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Clinical Scenario: A patient with a history of portal HTN presents with acute variceal bleeding. Your attending asks you to get GI to come in and perform emergent endoscopy. You call the GI expert who suggests starting Octreotide and Vasopressin and giving him a call with some follow-up in a few hours. He would prefer to scope the patient under less acute circumstances and wants you to manage the patient medically.

- P:** In ED patients with acute variceal bleeding
- I:** is emergent endoscopic therapy
- C:** compared with therapy with octreotide or terlipressin
- O:** associated with better outcomes.

Article	Study type	Patients	Outcomes	Positives	Negatives
<p>Authors D'Amico G, Pagliaro LLP, Pietrosi GGPI, Tarantino IITA</p> <p>Title Emergency sclerotherapy versus medical interventions for bleeding esophageal varices in cirrhotic patients</p> <p>Cochrane Database Syst Rev. 2002;(1):CD00223</p>	<p>Cochrane review</p> <p>Randomized clinical trials</p>	<p>Pts with acute bleeding from esophageal varices regardless of etiology or severity of liver disease</p> <p>Twelve trials including 1146 patients (pts) were identified.</p> <ul style="list-style-type: none"> • One trial compared sclerotherapy with vasopressin • one with terlipressin • four with somatostatin • six with octreotide. 	<p>No significant differences were found comparing sclerotherapy with each vasoactive drug for any outcomes.</p> <p>Adverse events (11 RCTs, 1082 pts) and serious adverse events (5 RCTs, 602 pts) were significantly more frequent with sclerotherapy: risk differences 0.08 (0.02 to 0.14) and 0.05 (0.02 to 0.08), respectively</p> <p>Combining all the trials irrespective of the vasoactive drug, risk differences (95% confidence intervals) were:</p> <ul style="list-style-type: none"> • failure to control bleeding (11 RCTs, 977 pts) -0.03 (-0.07 to 0.01) • five-day failure rate (7 RCTs, 759 pts) -0.05 (-0.12 to 0.01); • rebleeding (11 RCTs, 1082 pts) -0.01(-0.06 to 0.04) • rebleeding before other elective treatments (9 RCTs, 975 pts) -0.02 (-0.06 to 	<p>Reviewed a number of sources, including unpublished data, and symposiums</p> <p>RCTs</p> <p>Sclerosants and different endoscopic measurements were considered equivalent as no evidence has proven one superior to any other</p> <p>Separate meta analysis was conducted regarding the vasoactive agents as the data is unclear regarding the differences between them</p>	<p>2 independent reviews who chose studies included in the review were not blinded to authors, institutions, investigators, source, and results</p> <p>Didn't include blinding in quality assessment due to the difficulty of blinding sclerotherapy</p>

			<ul style="list-style-type: none"> 0.03) mortality (12 RCTs, 1146 pts) -0.04 (-0.08 to 0.00) mortality before other elective treatments (5 RCTs, 474 pts) -0.02 (-0.07 to 0.04) transfused blood units (7 RCTs, 793 pts) (weighted mean difference) -0.17 (-0.52 to 0.19). 		
<p>Authors Escorsell A, Del Arbol LR, Planas R, Albillos A, Banares R, Cales R, Pateron D, Bernard B, Vinel J, Bosch J</p> <p>Title Multicenter Randomized Controlled Trial of Terlipressin versus Sclerotherapy in the Treatment of Acute Variceal Bleeding: The TEST Study</p> <p>Hepatology. 2000 Sep;32(3):471-6</p>	Multicenter Randomized Control Trial	<p>219 cirrhotic patients with endoscopy-proven acute bleeding</p> <p>Randomized to receive repeated injections of terlipressin during 6 days or emergent sclerotherapy</p>	<p>Terlipressin injection is as effective as emergent sclerotherapy in controlling variceal bleeding and in preventing early rebleeding, with no significant differences in mortality, transfusion requirements, need for alternative treatments, and use of hospital resources.</p> <p>Less side effects associated with terlipressin Terlipressin 20% Sclerotherapy 30%</p>	<p>Computer generated randomization</p> <p>Initial assignment to either group occurred at initial diagnostic endoscopy</p>	<p>Band ligation is safer than injected sclerotherapy- this study looked at injection sclerotherapy</p>
<p>Authors R Planas, JC Quer, J Boix, M Armengol, E Cabre, T Pintanel, P Humbert, B Oller, MA Broggi et al</p> <p>Title A Prospective Randomized Trial Comparing Somatostatin and</p>	Prospective randomized	70 cirrhotic patients with esophageal variceal hemorrhage	<p>Mortality was no different in either group</p> <p>Sclerotherapy was associated with major complications resulting in the death of 2 patients</p>		Small study

<p>Sclerotherapy in the Treatment of Acute Variceal Bleeding</p> <p>Hepatology. 1994 Aug;20(2):370-5</p>					
<p>Authors SA Jenkins, R Shields, M Davies, E Elias, AJ Turnbull, MF Bassendine, OF James, JP Iredale, SK Vyas, MJ Arthur, AN Kingsnorth, R Sutton</p> <p>Title A multicenter randomized trial comparing octreotide and injection sclerotherapy in the management and outcome of variceal hemorrhage</p> <p>Gut 1997 Oct ;41(4):526-33</p>	<p>Multicenter Randomized</p>	<p>85 patients with acute variceal bleeding and 65 patients with recent hemodynamically significant variceal bleeding</p> <p>Randomized to sclerotherapy or octreotide infusion</p> <p>Medically treated pts underwent elective sclerotherapy at 48h</p> <p>Balloon tamponade was used in continued bleeding after sclerotherapy or hemodynamic instability in octreotide pts</p>	<p>Hemostasis rates, use of balloon tamponade, transfusion requirement, complications, and mortality after 48h were not significantly different</p> <p>Child's class nor the presence of active bleeding influenced the recurrent bleeding rates</p> <p>Trend, statistically insignificant, toward higher mortality in octreotide group</p> <p>Greater number of pts died of multiorgan dysfunction in octreotide group</p>	<p>Balloon tamponade for 12 h was the rescue tx for both groups</p> <p>Used a higher dose of octreotide than previous studies due to emerging evidence</p> <p>Follow up at 60d picked up new trend</p>	<p>Use of octreotide after endoscopic diagnosis of variceal bleeding</p> <p>9 patients had received injection sclerotherapy within 9-28 days</p> <p>Greater number of men and index bleeds in the octreotide group</p> <p>More active bleeders in sclerotherapy group</p>
<p>Authors Gross M, Scheimann U, Aulhoefer A, Zoller WG</p> <p>Title Meta-analysis: efficacy of therapeutic regimens in ongoing variceal bleeding</p> <p>Endoscopy. 2001 Sep;33(9):737-46</p>	<p>Medline search</p> <p>13 randomized controlled trials</p>	<p>Patients with ongoing variceal bleeding</p>	<p>Ligation appeared to be the most effective treatment (91.0 %, 95 % CI 82.4-96.3 %)</p> <p>Ligation was significantly more successful than vasoconstrictive treatment (vasopressin/terlipressin 68.7 %, 61.7-75.2 %; P < 0.002, chi-squared-test) or vasoactive treatment (somatostatin/octreotide, 75.9 %, 68.1-82.6 %; P < 0.02) treatment</p>	<p>Used Q test to exclude heterogeneity</p> <p>Calculations of estimated true effects, which take into account the weight of each study, produced similar results.</p>	<p>Ongoing bleeding is not usually the ED patient</p>

			Ligation was not statistically better than sclerotherapy (81.1 %, 71.7-88.4 %)		
<p>Authors Chen WC, Lo GH, Tsai WL, Hsu PI, Lin CK, Lai KH</p> <p>Title Emergency Endoscopic Variceal Ligation versus somatostatin for acute esophageal variceal bleeding</p> <p>[<i>J Chin Med Assoc</i> 2006;69(2):60–67]</p>	Randomized Prospective	<p>125 patients</p> <p>Cirrhosis</p> <p>Acute esophageal variceal bleeding presenting with hematemesis, melena or both</p> <p>Arrival to hospital within 12h</p> <p>No use of vasoactive drugs or endoscopy prior to referral to the study institution</p>	<p>Significantly higher rate of treatment failure in somatostatin group (20/63 pts or 21%) versus ligation (3/62 pts or 4%). Also confirmed the same for the subgroups of active vs nonactive bleeding</p> <p>Ligation group required less transfusion</p> <p>Trend, though not statistically significant, for shorter hospital stays in ligation group</p> <p>Adverse effects were not statistically different between the groups</p> <p>Mortality rate at 42days was 5 pts (8.1%) in ligation versus 3 pts (4.8%) in somatostatin</p>	<p>Computer-generated randomization</p> <p>2 groups with similar characteristics</p>	<p>After initial control of bleeding was established, each group was offered elective ligation or nadolol with isosorbide- not standardized so 42 day f/u was skewed</p> <p>NGT were used in somatostatin group but not in ligation group, therefore rebleed rates may be underestimated</p> <p>Somatostatin was started at or after diagnostic endoscopy so time lag may affect efficacy</p>
<p>Authors Stigman GV, Goff JS, Michaletz-Onody PA, Korula J, Lieberman D, Saeed ZA, Reveille RM, Sun JH, Lowenstein SR</p> <p>Title Endoscopic sclerotherapy as compared with endoscopic ligation for bleeding</p>	Randomized clinical trial	<p>129 patients with cirrhosis with proven bleeding from esophageal varices</p> <p>65- sclerotherapy and 64 with ligation</p> <p>Initial tx was followed by elective retreatment to eradicate varices</p>	<p>Active bleeding was controlled in 10/13 pt with sclerotherapy and 12/14 pts with ligation</p> <p>Eradication of varices required a lower mean of # of tx with ligation (4 +/-2) versus sclerotherapy (5 +/- 2)</p> <p>Mortality rate was significantly higher in sclerotherapy group 45% vs 28%, p=0.045</p>		<p>Small study</p> <p>Did not solely address single pt population (acute vs recent bleeds)</p>

<p>esophageal varices</p> <p>N Engl J Med. 1992 Jun 4;326(23):1527-32</p>			<p>Rate of complications was significantly higher in the sclerotherapy group 22% vs 2%, p=0.0001</p>		
<p>Authors Ioannou GN, Doust J, Rocky DC</p> <p>Title Terlipressin for acute esophageal variceal hemorrhage</p> <p>Cochrane Database Syst Rev. 2003;(1):CD002147</p>	<p>Cochrane Review Randomized clinical trials</p> <p>Searched Cochran Hepato-Biliary Group, Controlled Trials Register, The Cochran Controlled Trials Register on the Cochrane Library, MEDLINE, EMBASE, Biosis, Current Contents, experts in the field</p>	<p>20 studies with 1609 patients Documented or suspected bleeding from esophageal varices, cirrhosis, presenting with upper GI bleed</p> <ul style="list-style-type: none"> • 7 compared terlipressin to placebo • 3 compared terlipressin to somatostatin • 1 study compared terlipressin to endoscopy (219pts) <p>terlipressin compared to balloon tamponade, octreotide, and vasopressin</p>	<p>No statistically significant difference in terlipressin compared to other comparison groups in the number of adverse events that caused death or required the withdrawal of medication</p> <p>Author's conclusions:</p> <ul style="list-style-type: none"> • It is as safe as other treatments • It has demonstrated 34% relative reduction in mortality compared to no treatment • Insufficient data to determine whether it is better or worse than other available drugs or endoscopy. 	<p>Studies comparing terlipressin to balloon tamponade, octreotide, and vasopressin were of low quality, small</p> <p>Looked for unpublished data</p>	<p>Statistical heterogeneity in secondary outcomes (adverse events, early rebleeding, etc)</p> <p>Terlipressin vs placebo- 3 of the studies were performed after initial sclerotherapy</p> <p>Small studies therefore unable to elicit subtle differences between comparison groups</p>
<p>Authors Gotzche PC, Hrobjartsson</p> <p>Title Somatostatin analogues for acute bleeding in esophageal varices</p>	<p>Cochrane review</p> <p>Randomized placebo controlled trials</p> <p>Searched</p>	<p>21 trials 2588 patients suspected of acute or recent bleeding from esophageal varices</p>	<p>Did not reduce mortality significantly</p> <p>Number of patients failing initial hemostasis was reduced.</p> <p>Number of patients with rebleeding was not significantly reduced in trials with a low risk of bias while</p>	<p>Randomized with additional blinded analysis of data in many studies</p>	<p>Heterogeneity in the data- definitions of outcomes, dosages and lengths of administration of drugs</p> <p>Publication bias- saw several trials presented</p>

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Cochrane Database Syst Rev. 2008 Jul 16;(3):CD000193	PubMed, Cochrane Library, Cochrane Hepato-Biliary Group and its trial register. Any language, published and unpublished		significantly reduced in other trials Authors conclusions <ul style="list-style-type: none"> • ½ unit of blood saved per pt • Findings do not suggest a need for further placebo-controlled trials • 	as abstracts initially with change in data once published. 2 studies presented mortality as percentages which could not be correlated with the reported numerical data when checked.
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Clinical bottom line

Currently, the literature suggests that vasoactive drugs and endoscopic management are equally effective in controlling acute variceal bleeding. Newer studies are looking at combination therapy with both vasoactive agents and endoscopy. The first line choice of vasoactive agents remains under debate. Literature suggests that terlipressin and somatostatin are equally efficacious in controlling the acute bleed; however, terlipressin is the only agent proven by meta-analysis to reduce mortality. Similarly, more data is required in order to determine whether band ligation is superior to sclerotherapy.