



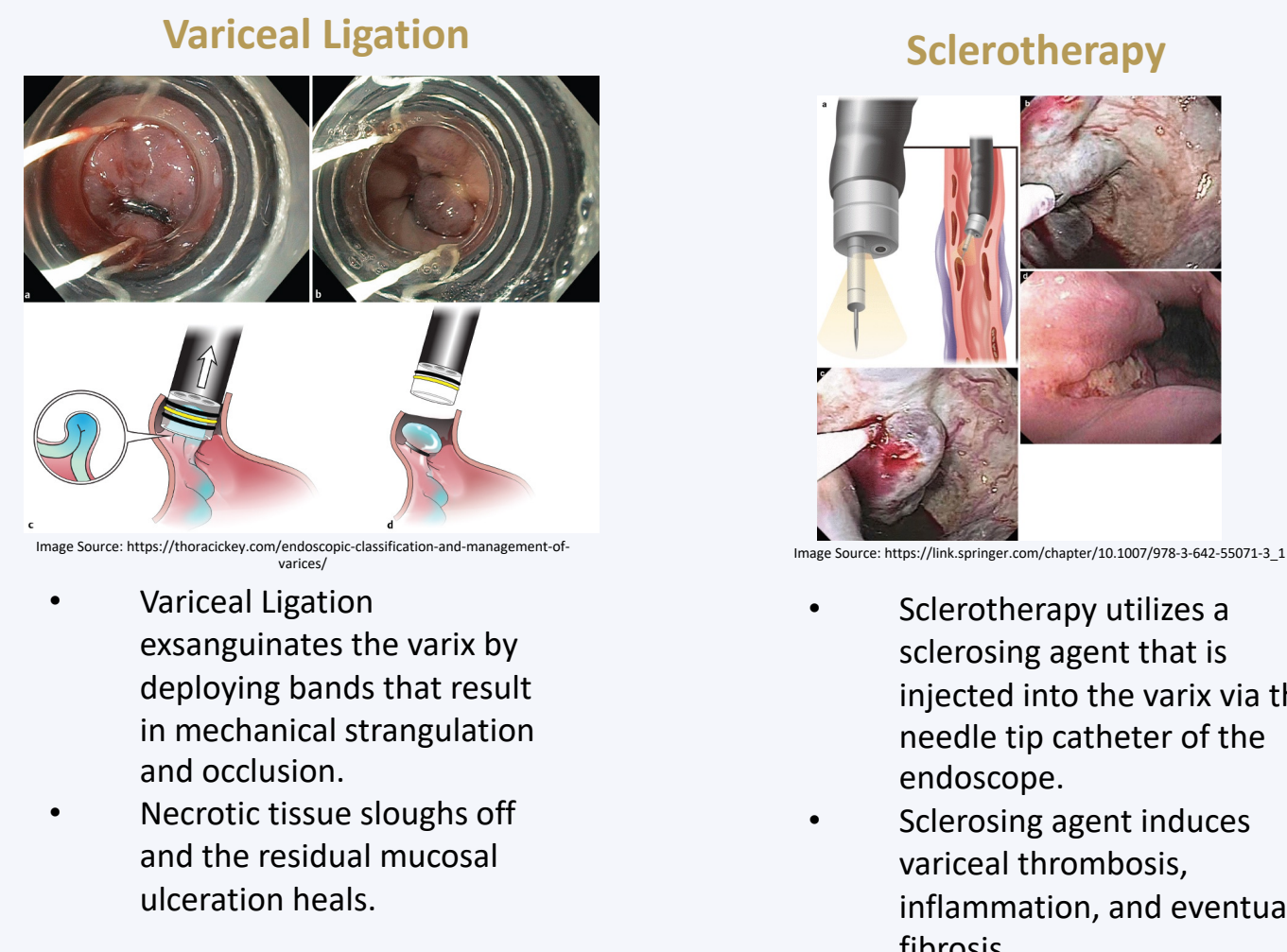
Purpose

Esophageal variceal bleeding is a potentially life-threatening complication of portal hypertension. Current guidelines recommend the use of endoscopic therapy for acute variceal bleed whereas Transjugular intrahepatic portosystemic shunt (TIPS) is used as secondary prophylaxis to prevent variceal rebleeding. Several studies have suggested that early TIPS, placed within 5 days of a variceal bleed, is associated with decreased rebleeding rates without significant increase in mortality. This study is an up-to-date systematic review with meta-analysis to evaluate the safety and efficacy of early TIPS versus endoscopic therapy in preventing variceal rebleeding in cirrhotic patients.

Materials and Methods

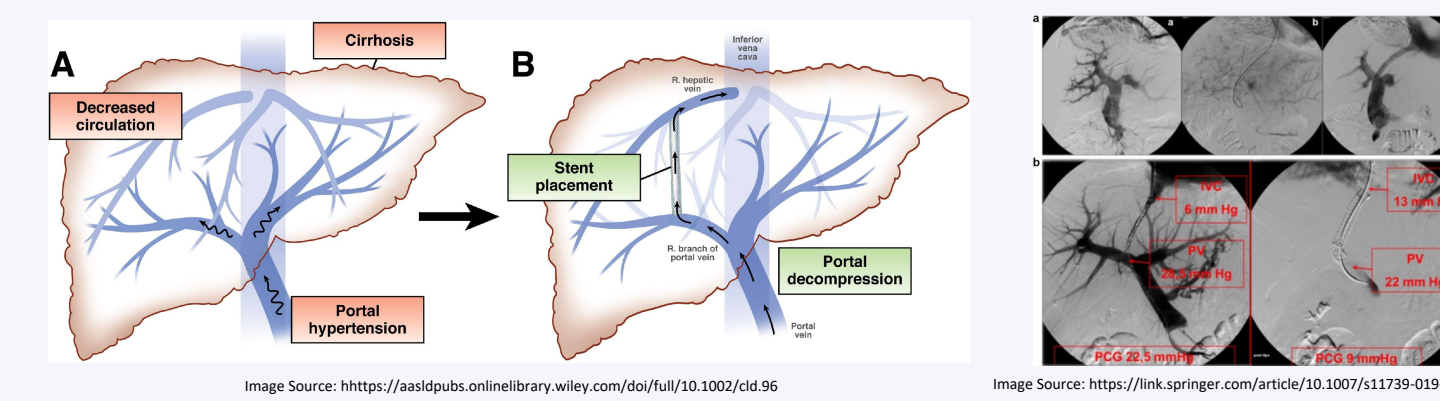
- Randomized controlled trials (RCT) comparing early TIPS to endoscopic therapy (variceal banding or sclerotherapy) were selected by searching Pubmed, Embase, Scopus, and Web of Science through September 2022.
- Inclusion criteria: randomized controlled trial, cirrhotic patients with prior episode of esophageal variceal bleed, patients who underwent early TIPS versus endoscopic therapy.
- Exclusion criteria: TIPS placement occurred more than 5 days after variceal bleed.
- Primary outcome: Mortality at 1 year.
- Secondary outcomes: Variceal rebleeding and hepatic encephalopathy at 1 year.
- Odds Ratio utilized for dichotomous data with 95% confidence interval
- Student's t-test used for statistical analysis and 2-tailed p values <0.05 were considered significant.

Endoscopic Therapy



- **Variceal Ligation** exsanguinates the varix by deploying bands that result in mechanical strangulation and occlusion. Necrotic tissue sloughs off and the residual mucosal ulceration heals.
- **Sclerotherapy** utilizes a sclerosing agent that is injected into the varix via the needle tip catheter of the endoscope. Sclerosing agent induces variceal thrombosis, inflammation, and eventual fibrosis.

Transjugular Intrahepatic Portosystemic Shunt (TIPS)



- TIPS involves the percutaneous insertion of a metal stent via the internal jugular vein to the hepatic vein and a channel is created through the hepatic parenchyma thereby connecting the hepatic vein to the portal vein.
- TIPS creates a portocaval shunt that significantly reduces the hepatic venous pressure gradient (HVPG).
- TIPS reduces variceal rebleeding more effectively compared to endoscopic therapy, however, the risk of hepatic encephalopathy may occur more frequently in TIPS compared to endoscopic therapy.¹
- Recent RCTs that evaluated the role of early TIPS (within 72 hrs of admission) in high-risk patients with acute variceal bleeding showed significant reduction in mortality and rebleeding without significant increase in PTE.

Results

Study	Total Number of Patients	Number of TIPS patients	Number of Endoscopy Patients	Mean Age (yrs)	Portal Hypertension Complication	Initial Intervention to Control the Active Esophageal Variceal Bleeding	Time of Randomization	Interval Between Randomization and Procedure	Types of TIPS Stent	Type of Endoscopic Therapy	Follow Up Time (months)
Cabrera et al. ¹	63	31	32	32	56 Active Esophageal Variceal Bleeding	Endoscopic Therapy	3 days after stabilization	Post-randomization	Uncovered Stent	Sclerotherapy	15 mo
Cello et al. ²	49	24	25	25	47 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Within 24 hrs of admission	Within 2 days	Uncovered Stent	Sclerotherapy	19 mo
Jalan et al. ³	58	31	27	27	57 Active Esophageal Variceal Bleeding	Endoscopic Therapy	24 hrs after stabilization	Post-randomization	Uncovered Stent	Single Band Ligation	16 mo
Rossle et al. ⁴	126	61	65	55	55 Active Esophageal Variceal Bleeding	Endoscopic Therapy	24 hours of admission	Within 2 days of admission	Uncovered Stent	Sclerotherapy and/or band ligation	TIPS - 14 mo Endoscopic Therapy - 13 mo
Sauer et al. ⁵	83	42	41	41	57 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Within 1-2 days of stabilization	Within 2 days	Uncovered Stent	Sclerotherapy	18 mo
Merli et al. ⁶	81	38	43	43	59 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Stratum I: < 7 days Stratum II: 1-6 wk Stratum III: 6-24 wk	Post-randomization	Uncovered Stent	Sclerotherapy	18 mo
Garcia-Villareal et al. ⁷	46	22	24	24	57 Active Esophageal Variceal Bleeding	Endoscopic Therapy	24 hrs after stabilization	Within 3 days	Uncovered Stent	Sclerotherapy	21 mo
Pomier-Layrargues et al. ⁸	80	41	39	39	54 Active Esophageal Variceal Bleeding	Endoscopic Therapy	24 hrs after stabilization	Within 3 days	Uncovered Stent	Single Band Ligation	TIPS - 22 mo Endoscopy - 19 mo
Sauer et al. ⁹	85	43	42	42	54 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Within 3 days of stabilization	Within 2 days	Uncovered Stent	Multiband Device	TIPS - 49 mo Endoscopy - 43 mo
Garcia-Pagan et al. ¹⁰	63	32	31	31	50 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Within 24 hrs of admission	Within 3 days	Polytetrafluoroethylene-Covered Stent	Multiband Device	16 mo
Lv et al. ¹¹	129	84	45	45	50 Active Esophageal Variceal Bleeding	Endoscopic Therapy	Within 24 hours of admission	Within 3 days	Covered Stent	Band Ligation or Sclerotherapy	24 mo

Table 1: Study Characteristics

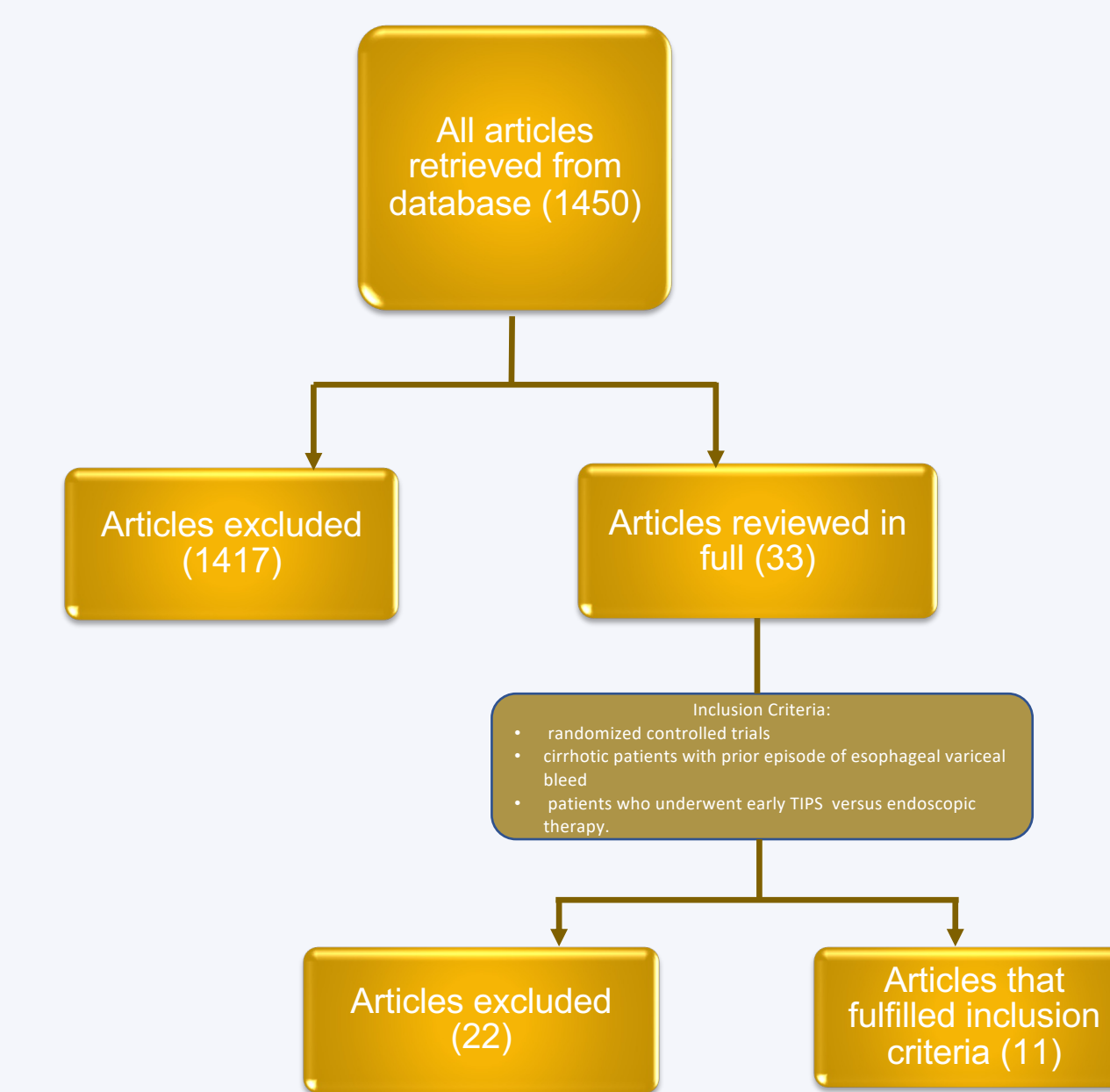


Figure 1: Schematic diagram of literature systematic review

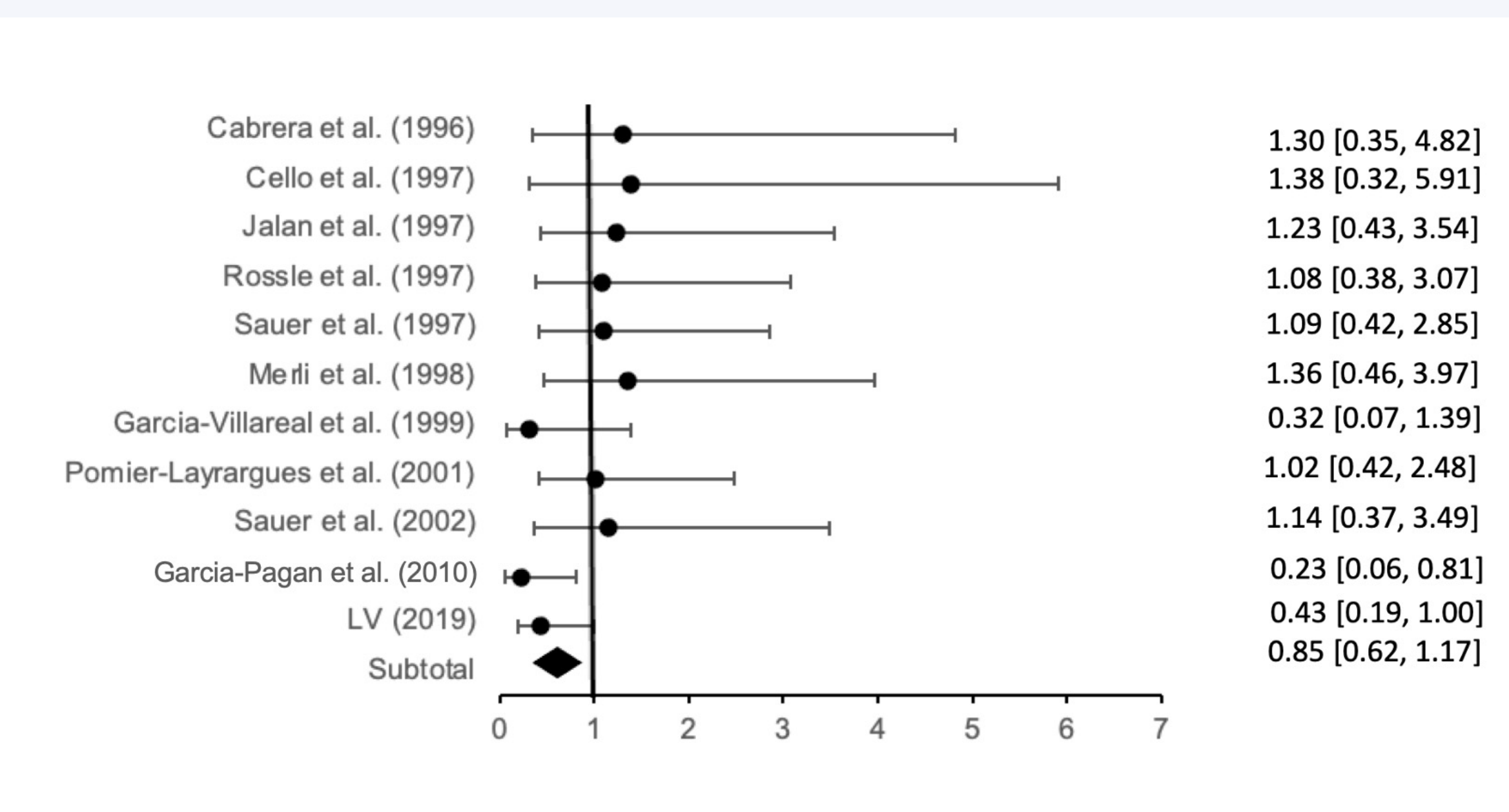


Figure 2: Meta-analysis of RCTs evaluating early TIPS versus endoscopic therapy for esophageal bleed; Odds Ratio and 95% CI for mortality at 1 year

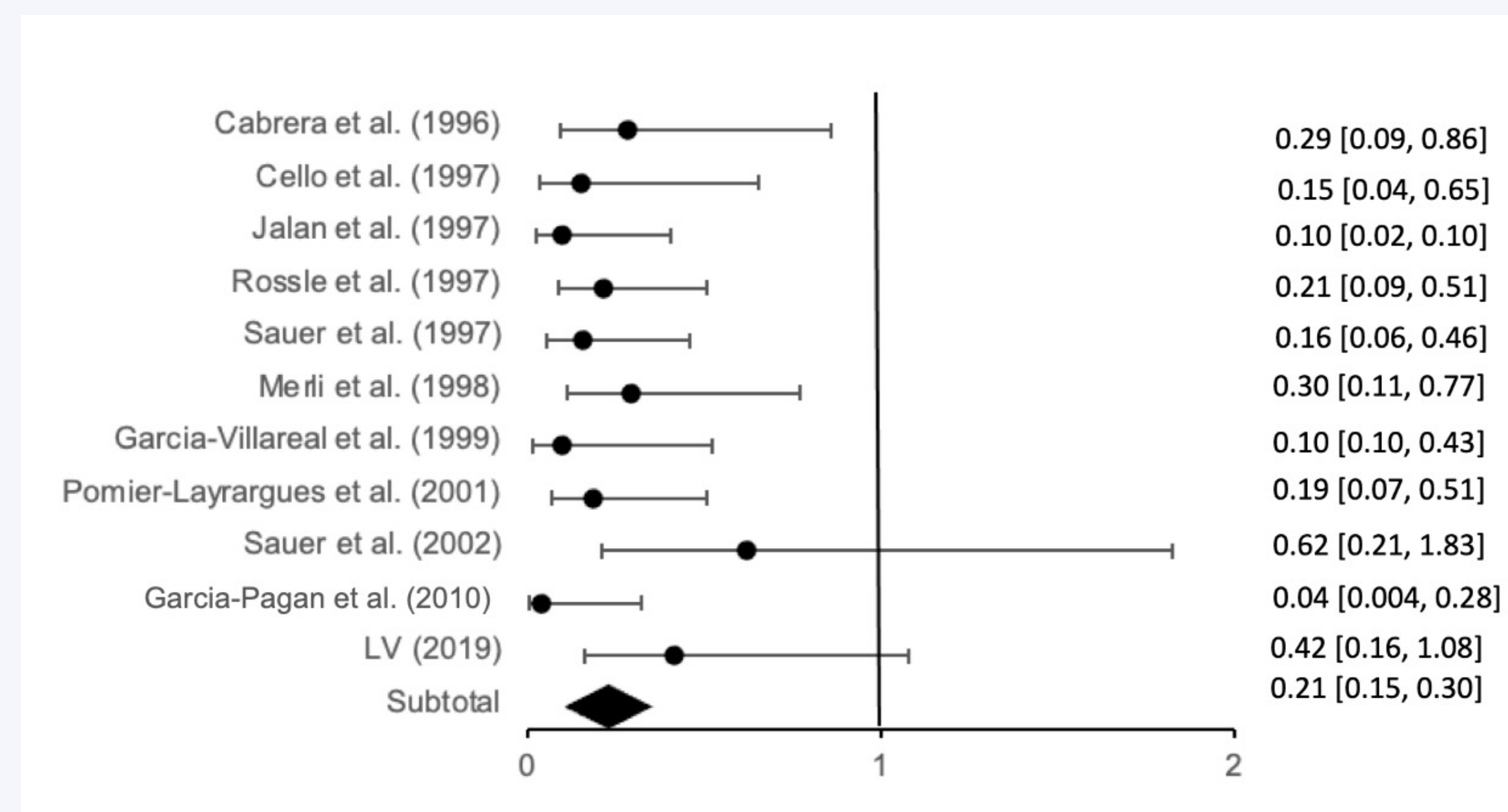


Figure 3: Meta-analysis of RCTs evaluating early TIPS versus endoscopic therapy for esophageal bleed; Odds Ratio and 95% CI for variceal rebleeding

Results cont'd

- Eleven randomized controlled trials included 861 patients with cirrhosis.
- All studies initially utilized endoscopic therapy for control of acute variceal bleed.
- The average follow-up time was 21 months.
- Mortality at 1 year occurred in 100 of 450 patients in the early TIPS group (22.2%) versus 104 of 414 (25.12%) in the endoscopic therapy group. There was no significant difference in mortality at 1 year. (OR = 0.85 [(95% CI 0.62, 1.17); P = 0.46; Figure 2]).
- Significantly lower rates of variceal rebleeding in the early TIPS group (pooled OR = 0.21[(95% CI 0.15-0.30); P < 0.001; Figure 3])
- No significant difference in the incidence of hepatic encephalopathy at 1 year. (P=0.08).

Conclusion

Early TIPS is superior to endoscopic therapy in preventing variceal rebleed in cirrhotic patients without significantly increasing the rate of mortality or hepatic encephalopathy.

References:

