

**Supplementary Table 1. Methodological quality of the trials included**

<b>Author, year, reference</b>	<b>Generation of allocation sequence *</b>	<b>Allocation concealment +</b>	<b>Successful randomization ‡</b>	<b>Investigator blinding †</b>	<b>Intention to treat analysis §</b>	<b>Withdrawals and Dropouts ¶</b>
<b>Endoscopic variceal ligation (EVL) and Beta-blockers (BB) vs. BB</b>						
Ahmad, 2009 (18)	Adequate	Yes	Yes	No	No	Yes
Lo, 2009 (22)	Adequate	Yes	Yes	No	Yes	Yes
García-Pagán, 2009 (23)	Adequate	Yes	Yes	No	Yes	Yes
<b>Endoscopic variceal ligation (EVL) and Beta-blockers (BB) vs. EVL</b>						
Ahmad, 2009 (18)	Adequate	Yes	Yes	No	No	Yes
Kumar, 2009 (19)	Adequate	Yes	Yes	No (only endoscopist blinded)	No	Yes
De la Peña, 2006 (20)	Adequate	Yes	Yes	No	Yes	Yes
Lo, 2000 (21)	Adequate	Yes	Yes	No	Yes	Yes

\* Allocation considered adequate when the sequence of random numbers was computer-generated.

+ Method used (central randomization, sealed envelopes) prevented the investigators from knowing which treatments was next before allocation.

‡ Balance existed between the baseline characteristics of the treatment and control groups.

† Blinding of therapies explicitly mentioned in the report.

§ Explicit mention in the report that all randomized patients were analyzed in the group to which they were originally allocated, regardless of the treatment received (intention-to-treat principle).

¶ Numbers and reasons provided in the report.

**Supplementary table 2. Patients included in the final database and individual reasons for exclusion for each outcome.**

Study, year, reference	Patients from the original studies	Reasons for exclusion of the final database	Patients included in the final analyses	Allocation to treatment groups	Number of patients excluded for time- to-event analysis			Number of patients included for analysis for each outcome		
					Overall rebleeding	Variceal rebleeding	Mortality	Overall rebleeding	Variceal rebleeding	Mortality
Endoscopic variceal ligation (EVL) and beta-blockers (BB) vs. BB										
Ahmad, 2009 (18)	150	39 allocated in the EVL group	111	EVL+BB: 37 BB: 74	111 without time-to-event	111 without time-to-event	0	0	0	111
Lo 2009 (22)	120	0	120	EVL+BB: 60 BB: 60	0	0	0	120	120	120
Garcia- Pagan 2009 (23)	158	0	158	EVL+BB: 80 BB: 78	0	0	0	158	158	158
Endoscopic variceal ligation (EVL) and beta-blockers (BB) vs. EVL										
Ahmad, 2009 (18)	150	74 allocated in the BB group	76	EVL+BB: 37 EVL: 39	76 without time-to-event	76 without time-to-event	0	0	0	76
Kumar, 2009 (19)	177	10 without follow-up in the original database + 26 with non- cirrhotic portal hypertension	141	EVL+BB: 72 EVL: 69	0	0	0	141	141	141
De la Peña, 2005 (20)	80	1 without clinical data in the original database	79	EVL+BB: 43 EVL: 36	0	0	0	79	79	79
Lo, 2000 (21)	122	2 without Child in the original database	120	EVL+BB: 58 EVL: 62	9 without time-to-event	120 without information of rebleeding source	0	111	0	120

**Supplementary table 3. Characteristics of the patients allocated to each treatment group of each RCT included.**

Author, year, ref.	Number of patients	Allocation to treatment groups	Age (mean±SD or range)	Sex Male/female (%)	Etiology (alcohol/virus) (%)	Child A/B-C (%)	Child Score (mean±SD)
Endoscopic variceal ligation (EVL) and beta-blockers (BB) vs. BB							
Ahmad, 2009 (18)	111	BB+EVL: 37	50 (11)	81/19	0/100	11/89	8.2 (2)
		BB: 74	52 (9)	62/38	0/100	11/89	8.8 (2)
Lo, 2009 (22)	120	BB+EVL: 60	54 (10)	70/30	35/21	33/67	NA
		BB: 60	52 (11)	75/25	25/66	35/65	NA
García-Pagán, 2009 (23)	158	BB+EVL: 80	57 (12)	81/19	39/34	20/80	8.2 (1.8)
		BB: 78	56 (11)	68/22	42/28	23/77	8.1 (1.8)
Endoscopic variceal ligation (EVL) and beta-blockers (BB) vs. EVL							
Ahmad, 2009 (18)	76	BB+EVL: 37	50 (11)	81/19	0/100	11/89	8.2 (2)
		EVL: 39	53(10)	64/36	3/97	18/82	8.3 (2)
Kumar, 2009 (19)	141	BB+EVL: 72	41(14)	85/15	43/17	46/54	7.3 (2)
		EVL: 69	41(13)	88/12	40/27	35/65	7.8 (2.1)
De la Peña, 2005 (20)	79	BB+EVL: 43	60 (36-75)	77/23	63/28	14/86	NA
		EVL: 36.	60 (18-75)	73/27	70/22	16/84	NA
Lo, 2000 (21)	122	BB+EVL: 60	53 (11)	75/25	28/68	18/82	NA
		EVL: 62	51 (12)	80/20	32/66	29/71	NA

**Supplementary table 4**

**Exploratory analysis of the effect of the association of isosorbide-5-mononitrate (ISMN) to beta-blockers (BB) in trials comparing combination endoscopic variceal ligation (EVL) and BB versus EVL alone**

		Effect of the type of drug	
		OR (95% CI)	P-Value <sup>a</sup>
Death	BB+EVL vs EVL	0.332 (0.143; 0.77)	0.243
	BB+ISMN+EVL vs EVL	0.717 (0.269; 1.914)	
All-source rebleeding	BB+EVL vs EVL	0.228 (0.116; 0.451)	0.007
	BB+ISMN+EVL vs EVL	0.828 (0.438; 1.563)	
Variceal rebleeding	BB+EVL vs EVL	0.223 (0.055; 0.903)	0.114
	BB+ISMN+EVL vs EVL	0.788 (0.389; 1.597)	

<sup>a</sup> P-Value for between-groups and therapy interaction