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Self-expanding metal stents versus TIPS in treatment of refractory bleeding esophageal varices: a systematic review and meta-analysis

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ABSTRACT

Background and study aims Refractory and recurrent esophageal variceal (EV) bleeding can be life threatening. Self-expanding metal stents (SEMS) have been used as a "bridge" therapy. However, their role in the treatment protocol is not established due to paucity in data.

Methods We searched multiple databases from inception through May 2019 to identify studies that reported on SEMS and TIPS in refractory EV hemorrhage. Our primary goals were to analyze and compare the pooled all-cause mortality, immediate bleeding control and rebleeding rates.

Results Five hundred forty-seven patients from 21 studies were analyzed (SEMS: 12 studies, 176 patients; TIPS: 9 studies, 398 patients). The pooled rate of all-cause mortality with SEMS was 43.6 % (95 % CI 28.6–59.8, I^2 = 38) and with TIPS was 27.9 % (95 % CI 16.3–43.6, I^2 = 91). The pooled rate of immediate bleeding control with SEMS was 84.5 % (95 % CI 74–91.2, I^2 = 40) and with TIPS was 97.9 % (95 % CI 87.7–99.7, I^2 = 0). The pooled rate of rebleeding with SEMS was 19.4 % (95 % CI 11.9–30.4, I^2 = 32) and with TIPS was 8.8 % (95 % CI 4.8–15.7, I^2 = 40).

Conclusion Use of SEMS in refractory EV hemorrhage demonstrates acceptable immediate bleeding control with good technical success rate. Mortality and rebleeding rates were lesser with TIPS, however, its superiority and/ or inferiority cannot be validated due to limitations in the comparison methodology.

Introduction

Esophageal variceal (EV) bleeding is one of the most life-threatening complications of portal hypertension, with mortality rates of 15 % to 20 % [1]. The current recommendation is to hemodynamically stabilize the patient and promptly initiate vasoactive drugs like terlipressin and/or somatostatin analogues, followed by endoscopic ligation of EV, ideally within 12 hours of presentation [2, 3]. However, 20 % to 30 % of patients can rebleed and become refractory to standard treatment [4].

In refractory patients, treatment options include surgical and/or non-surgical creation of a porto-systemic shunt that reduces the portal pressure and controlling the bleeding by tamponade. Surgical options of shunt creation are as follows: portocaval (portal vein and vena cava), mesocaval (mesenteric vein and vena cava), spleno-renal shunt (proximal splenic vein and left renal vein), and externally reinforced shunts that can be either mesocaval or portocaval. Non-surgical options include balloon tamponade, trans-jugular intra-hepatic porto-systemic shunt (TIPS) that is created by an interventional radiologist under fluoroscopic guidance and the placement of a self-expanding metal stent (SEMS) [2, 3].

Balloon tamponade was the most commonly used option in the past. However, it has fallen out of favor due to risk of pressure-induced necrosis of the esophagus and to the fact that it can only be used for, at most, 24–48 hours [5]. Use of TIPS is limited by technical difficulties and availability [6]. Studies published thus far report the use of SEMS as a 'bridge' therapy with majority of the patients eventually being treated with EV banding and/ or TIPS [3, 7–9]. Although the current Baveno consensus workshop recommends the use of SEMS, an evidence-based approach to guide the use of SEMS in potentially life-threatening refractory EV bleeding is not established.

The goals of this meta-analysis were to study the clinical outcomes of SEMS, and use the clinical outcomes of TIPS as a comparator, in refractory EV hemorrhage.

Methods

Search strategy

We conducted a comprehensive search of several databases from inception to May 24, 2019. The databases included Ovid MEDLINE® and Epub Ahead of Print, In-Process and other non-indexed citations, Ovid Embase, Ovid Cochrane Central Register of Controlled trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. An experienced medical librarian using inputs from the study authors helped with the literature search. Controlled vocabulary supplemented with keywords was used to search for studies of interest. The full search strategy is available in **Appendix 1**. The PRISMA and MOOSE checklist were followed and are provided in **Appendix 2** and **3** [10, 11].

Study selection

In this meta-analysis, we included studies that evaluated clinical outcomes of SEMS and studies that evaluated outcomes of TIPS in patients with refractory EV hemorrhage. Studies were included irrespective of the study sample-size, inpatient/outpatient setting, and geography as long as they provided data needed for the analysis.

Studies done in the pediatric population (age < 18 years), and studies not published in English language were our only exclusion criteria. In case of multiple publications from the same cohort and/or overlapping cohorts, data from the most recent and/or most appropriate comprehensive report were retained.

Data abstraction and quality assessment

Data on study-related outcomes in individual studies were abstracted onto a standardized form by at least two authors (SRK, RK), and two authors (BPM, SC) did the quality scoring independently. Primary study authors were contacted via email as needed for further information and/or clarification on data.

The Newcastle-Ottawa scale for cohort studies was used to assess the quality of studies [12]. This quality score consisted of 8 questions, the details of which are provided in **Supplementary Table 1**.

Outcomes assessed

1. Pooled rate of all-cause mortality,
2. Pooled rate of immediate EV bleeding control,
3. Pooled rate of rebleeding, and
4. Pooled rate of adverse events.

Comparison analysis: The outcomes with SEMS were compared with the outcomes of TIPS.

Assessment methodology and definitions

The collected data was matched between the groups (SEMS and TIPS) before statistical analysis. Although, this model of comparison is indirect, the approach is comparable to a retrospective case-control study with matched groups [13]. Refractory EV bleeding was defined according to the Baveno IV and V guidelines: fresh hematemesis or aspiration of > 100 ml of fresh blood via the nasogastric tube beyond 2 hours after endoscopy and/or a drop of 3 g/dL in hemoglobin without blood transfusion [5, 14].

Rebleeding was defined as per the Baveno V guidelines: evidence of rebleeding from portal hypertensive sources (hematemesis, malena, aspiration of > 100 mL of fresh blood via the nasogastric tube beyond two hours after endoscopy and/or a drop of 3 g/dL in hemoglobin without blood transfusion [14].

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimates in each case following the methods suggested by DerSimonian and Laird using the random-effects model [15]. When incidence of an outcome was zero in a study, a continuity correction of 0.5 was added to the number of incident cases before statistical analysis [16]. We assessed heterogeneity between study-specific estimates by using Cochran Q statistical test for heterogeneity, 95 % prediction interval (PI), which deals with the dispersion of the effects [17–19]. and the I^2 statistics [20, 21]. In this, values < 30 %, 30 % to 60 %, 61 % to 75 %, and > 75 % were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively [22]. Publication bias was as-

▶ **Table 1** Study and population characteristics.

Study	Design, period, center, country	Intervention	Age (years)	Total patients (n)	M/F	Meld	Child–Pugh score	Rebleeding	Mortality (all-cause)	Adverse events – total	Stent migration	Stent indwell time	Follow-up (d = days)
Dechene, 2012 [26]	Retrospective Case series, August 2007 to March 2011, Single center, Germany.	SEMS	63.8 (11)	8	6/2	29.37 (16–40)	A: 0, B:0, C:8	3	5n (60 d); 6n (Total)	0	0	11 d (4–17 d)	60 d
Drastich, 2016 [27]	Retrospective Case series, Jun 2011 to Nov 2014, Single Center, Czech Republic.	SEMS	52.9 (27–80)	14	7/7	nr	nr	nr	7	nr	2/13	9.5 d (7–26 d)	nr
Escorsell, 2016 [28]	Randomised controlled trial, March 2009 to January 2013 Multicenter, Spain.	SEMS	69 (40–81)	13	13/0	16.5 (9–32)	A:3, B:10, C:10	2/13 (15 d), 6/13 (42 d)	6n (42 d)	6	7	7 d (2–14 d)	42 d (6-weeks)
Fierz, 2013 [29]	Retrospective Case series, Oct 2010 to Oct 2011, Multicenter, Switzerland.	SEMS	57 (41–68)	7	5/2	27 (11–37)	A:0, B: 2, C: 5	0	2n (42 d)	2	2	12 h–5 d	42 d
Goenka, 2017 [7]	Retrospective, Apr 2012 to May 2016, Single center, India.	SEMS	53 ± 13.7 (27 to 72)	12	11/1	20.17 ± 5.97 (14 to 35)	nr	1	5	0	0	17.5 d (7–30 d)	30 d
Holster, 2013 [8]	Prospective Case series, Feb 2012 to Oct 2012, Single center, Netherlands.	SEMS	58 (48–78)	5	3/2	21 (11–28)	A:1, B:1, C:1	1	3	1	1	11 d (6–214 d)	180 d (6 months)
Muller, 2015 [31]	Retrospective Case series, May 2011 to Mar 2014, Single center, Germany.	SEMS	64.2 (43–79)	11	8/3	16 (8–36)	A:1, B:6, C:3	1	3 (42 d)	9	7	12.1 d (5–24 d)	42 d
Mishin, 2013 [30]	Retrospective Case series, Moldova.	SEMS	46.92 (24–62)	12	8/4	nr	nr	1	3	5	5	nr	30 d
Pfisterer, 2019 [9]	Retrospective, Jan 2009 to Dec 2016, Multicenter, Austria.	SEMS	55.5 (SD 11.5)	34	28/6	Median = 18 (IQR 10)	A:1, B:10, C:8	22	22	17	13	5 d (pt survived ≥ 14 days)	42 d (6 weeks)

▶ **Table 1** (Continuation)

Study	Design, period, center, country	Intervention	Age (years)	Total patients (n)	M/F	Meld	Child–Pugh score	Rebleeding	Mortality (all-cause)	Adverse events – total	Stent migration	Stent indwell time	Follow-up (d = days)
Wright, 2010 [32]	Retrospective Case series, Mar 2007 to Jul 2008, Single center, United Kingdom.	SEMS	49.4 (18–70)	10	9/1	32 (23–39)	nr	3	5 (42 d)	1	0	9 d (6–14 d)	42 d
Zakaria, 2013 [33]	Retrospective Case series, Jan 2008 to Dec 2009, Single center, Egypt.	SEMS	55.60 ± 5.62 (18–65)	16	14/2	nr	A:2, B:8, C:6	2	4	7	6	2–4 d	nr
Zehetner, 2008 [34]	Retrospective, Jan 2003 to Aug 2006, Austria.	SEMS	56 (32–91)	34	33/1	nr	A:0, B:13, C:21	0	10 (60 d)	8	7	5 d (1–14 d)	60 d
Cello, 1997 [35]	Randomised controlled trial, Nov 1991 to Dec 1995, Multicenter, USA.	TIPS	48.8 (2.0)	24	19/5	nr	nr	3	5n (30 d)	nr	nr	nr	574.5 ± 109 d
Garcia-Pagan, 2010 [6]	Randomised controlled trial, May 2004 to Mar 2007, Spain.	TIPS	52 ± 10	32	21/11	15.5 ± 5	A:0, B:16, C:16	0	4	nr	nr	nr	14.6 ± 8.4 months
Garcia-Pagan, 2013 [36]	Retrospective (Randomised controlled trial), Mar 2007 to Jan 2011, Spain.	TIPS	56 ± 12	45	34/11	16.5 ± 5	A:0, B:18, C:27	2	6	nr	nr	nr	13.1 ± 12 months
Monescillo, 2004 [37]	Randomised controlled trial, Jun 1997 to Nov 2000, Single center, Spain.	TIPS	56 ± 12 (32–75)	26	22/4	nr	A:3, B:11, C:12	3	8	nr	nr	nr	1 years
Orloff, 2012 [42]	Prospective Randomized controlled trial, Jul 1996 to Jul 2011, USA.	TIPS	49 (30–84)	78	56/22	nr	A:16, B:39, C:23	nr	66	nr	nr	nr	3 to 10 years
Popovic, 2010 [38]	Retrospective, Apr 1994 to Jan 2000, Single center, Slovenia.	TIPS	52.0 ± 13.2	50	29/21	nr	A:8, B:26, C:16	3	13	16	nr	nr	35.5 ± 19.6 months
Rudler, 2014 [39]	Prospective, Mar 2011 to Feb 2013, Single center, France.	TIPS	53.2 ± 9.0	31	24/7	20.9 ± 6.9	A:0, B:7, C:24	0	9	14	nr	nr	7.8 months

▲ **Table 1** (Continuation)

Study	Design, period, center, country	Intervention	Age (years)	Total patients (n)	M/F	Meld	Child–Pugh score	Rebleeding	Mortality (all-cause)	Adverse events – total	Stent migration	Stent indwell time	Follow-up (d = days)
Shi, 2014 [40]	Retrospective, Jan 2006 to Dec 2011, Single center, China	TIPS	49.7 ± 9.0	48	30/18	NR	A:11, B:28, C:9	9	16	23	nr	nr	35.4 ± 18.7 months
Xue, 2012 [41]	Retrospective, Jan 2007 to Jun 2010, Single center, China	TIPS	51 ± 13	64	42/22	NR	A:23, B:30, C:11	nr	8	nr	nr	nr	20.7 ± 1.3 months

SEMS, self-expanding metal stent; TIPS, transjugular intrahepatic portosystemic stent; MELD. model for endstage liver disease, nr, not reported

certained, qualitatively, by visual inspection of funnel plot and quantitatively, by the Egger test [23]. When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie's "Trim and Fill" test was used to ascertain the impact of the bias [24]. Three levels of impact were reported based on the concordance between the reported results and the actual estimate if there were no bias. The impact was reported as minimal if both versions were estimated to be same, modest if effect size changed substantially but the final finding would still remain the same, and severe if basic final conclusion of the analysis is threatened by the bias [25].

All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 3 (BioStat, Englewood, New Jersey, United States).

Results

Search results and population characteristics

From an initial 395 studies, 214 records were screened and 33 full-length articles were assessed. Twenty-one studies were included in the final analysis, of which 12 studies reported on the outcomes with SEMS [7–9, 26–34] and 9 reported on the outcomes with TIPS [6, 35–42].

The schematic diagram of study selection is illustrated in **Supplementary Fig. 1**. Two SEMS studies had cohort overlap and the most comprehensive one was retained for the analysis (Wright 2010 with Hogan 2009 and Zehetner 2008 with Hubmann 2006) [32, 34, 43, 44].

Baseline population characteristics were comparable between the SEMS and TIPS groups. The mean and/or median age ranged from 46 years to 69 years, with a predominantly male population (74 %). Twelve percent of the patients were Child's A, 39 % were Child's B and the rest were Child's C cirrhotics. The mean MELD score ranged from 16 to 29.37 in SEMS group and 15.5 to 20.9 in TIPS groups. The ELLA-CS stent (SX-ELLA Stent Danis, Hradec Kralove, Czech Republic) was used in all SEMS studies with a stent indwell time ranging from 1 to 30 days. Data was not available on the severity of the bleeding and the interventional procedure was done on an emergency basis. The population characteristics are described in ▶ **Table 1**.

Characteristics and quality of included studies

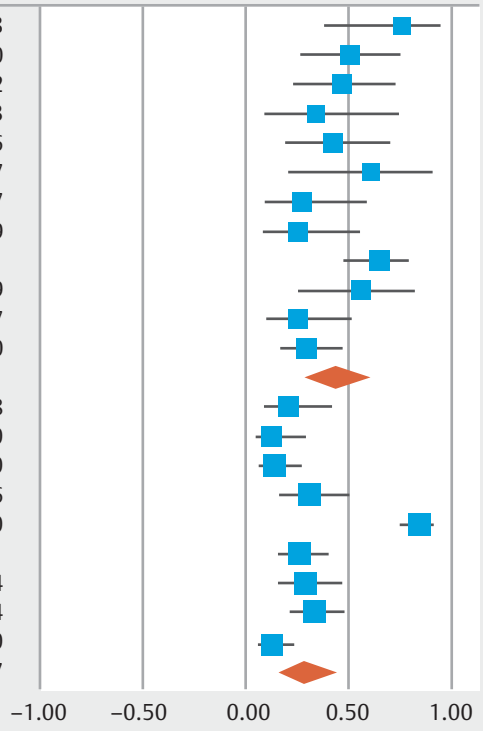
One SEMS study was prospective, whereas rest were retrospective [8]. Three were from multicenter data [9, 28, 29]. No studies were population-based. Overall, four studies were considered high quality and the rest were medium quality [9, 28, 29, 34]. There were no low-quality studies. All TIPS studies in the comparator group were considered high quality. The detailed assessment of study quality can be found in **Supplementary Table 1**.

Meta-analysis outcomes

A total of 574 patients were included in the analysis from 21 studies. 176 patients were treated with SEMS in 12 studies and 398 patients were treated with TIPS in 9 studies.

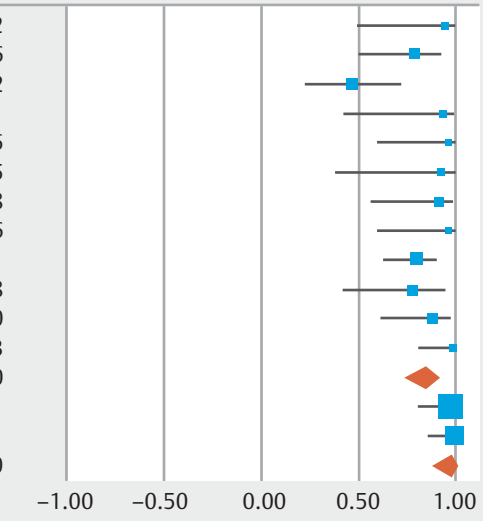
The pooled rate of all-cause mortality with SEMS was 43.6 % (95 % CI 28.6–59.8) and with TIPS was 27.9 % (95 % CI 16.3–

Group by intervention	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
SEMS	Dechene, 2012	0.750	0.377	0.937	1.346	0.178
SEMS	Drastich, 2016	0.500	0.260	0.740	0.000	1.000
SEMS	Escorsell, 2016	0.462	0.224	0.718	−0.277	0.782
SEMS	Fierz, 2013	0.333	0.084	0.732	−0.800	0.423
SEMS	Goenka, 2017	0.417	0.185	0.692	−0.575	0.566
SEMS	Holster, 2013	0.600	0.200	0.900	0.444	0.657
SEMS	Muller, 2015	0.273	0.090	0.586	−1.449	0.147
SEMS	Mishin, 2013	0.250	0.083	0.522	−1.648	0.099
SEMS	Pfisterer, 2019	0.647	0.476	0.787	1.689	0.091
SEMS	Wright, 2010	0.556	0.251	0.823	0.333	0.739
SEMS	Zakaria, 2013	0.250	0.097	0.508	−1.903	0.057
SEMS	Zehetner, 2008	0.294	0.166	0.466	−2.326	0.020
SEMS		0.436	0.286	0.598	−0.771	0.441
TIPS	Cello, 1997	0.208	0.089	0.413	−2.656	0.008
TIPS	Garcia-Pagan, 2010	0.125	0.048	0.289	−3.640	0.000
TIPS	Garcia-Pagan, 2013	0.133	0.061	0.267	−4.268	0.000
TIPS	Monescillo, 2004	0.308	0.162	0.505	−1.908	0.056
TIPS	Orloff, 2012	0.846	0.748	0.911	5.432	0.000
TIPS	Popovic, 2010	0.260	0.157	0.398	−3.244	0.001
TIPS	Rudler, 2014	0.290	0.159	0.470	−2.259	0.024
TIPS	Shi, 2014	0.333	0.215	0.477	−2.264	0.024
TIPS	Xue, 2012	0.125	0.064	0.231	−5.148	0.000
TIPS		0.279	0.163	0.436	−2.691	0.007



▶ **Fig. 1** Forest plot, mortality.

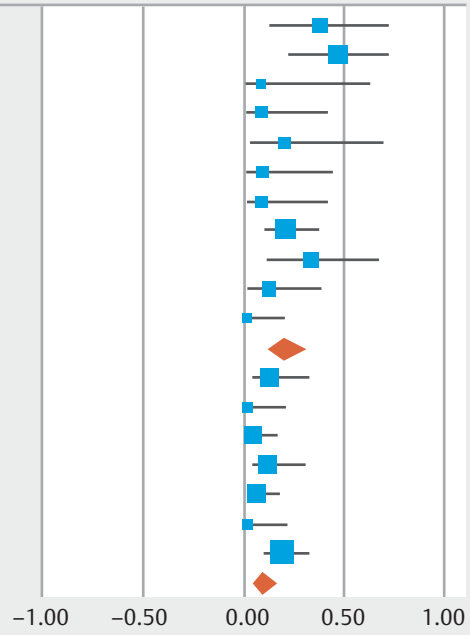
Group by intervention	Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value
SEMS	Dechene, 2012	0.944	0.495	0.997	1.947	0.052
SEMS	Drastich, 2016	0.786	0.506	0.929	1.995	0.046
SEMS	Escorsell, 2016	0.462	0.224	0.718	−0.277	0.782
SEMS	Fierz, 2013	0.929	0.423	0.996	1.748	0.081
SEMS	Goenka, 2017	0.962	0.597	0.998	2.232	0.026
SEMS	Holster, 2013	0.917	0.378	0.995	1.623	0.105
SEMS	Muller, 2015	0.909	0.561	0.987	2.195	0.028
SEMS	Mishin, 2013	0.962	0.597	0.998	2.232	0.026
SEMS	Pfisterer, 2019	0.794	0.627	0.899	3.183	0.001
SEMS	Wright, 2010	0.778	0.421	0.944	1.562	0.118
SEMS	Zakaria, 2013	0.875	0.614	0.969	2.574	0.010
SEMS	Zehetner, 2008	0.986	0.809	0.999	2.973	0.023
SEMS		0.845	0.740	0.912	5.125	0.000
TIPS	Rudler, 2014	0.968	0.804	0.995	3.346	0.001
TIPS	Shi, 2014	0.990	0.857	0.999	3.218	0.001
TIPS		0.979	0.877	0.997	4.017	0.000



▶ **Fig. 2** Forest plot, immediate bleeding control.

43.6) (▶ **Fig. 1**). The pooled rate of immediate bleeding control with SEMS was 84.5% (95% CI 74–91.2) and with TIPS was 97.9 % (95% CI 87.7–99.7) (▶ **Fig. 2**). The pooled rate of re-bleeding with SEMS was 19.4% (95% CI 11.9–30.4) and with TIPS was 8.8% (95% CI 4.8–15.7) (▶ **Fig. 3**).

Group by intervention	Study name	Statistics for each study					Event rate and 95% CI
		Event rate	Lower limit	Upper limit	Z-Value	p-Value	
SEMS	Dechene, 2012	0.375	0.125	0.715	−0.699	0.484	
SEMS	Escorsell, 2016	0.462	0.224	0.718	−0.277	0.782	
SEMS	Fierz, 2013	0.083	0.005	0.622	−1.623	0.105	
SEMS	Goenka, 2017	0.083	0.012	0.413	−2.296	0.022	
SEMS	Holster, 2013	0.200	0.027	0.691	2.195	0.028	
SEMS	Muller, 2015	0.091	0.013	0.439	−2.195	0.028	
SEMS	Mishin, 2013	0.083	0.012	0.413	−2.296	0.022	
SEMS	Pfisterer, 2019	0.206	0.101	0.373	−3.183	0.001	
SEMS	Wright, 2010	0.333	0.111	0.667	−0.980	0.327	
SEMS	Zakaria, 2013	0.125	0.031	0.386	−2.574	0.010	
SEMS	Zehetner, 2008	0.015	0.001	0.386	−2.951	0.003	
SEMS		0.195	0.119	0.304	−4.709	0.000	
TIPS	Cello, 1997	0.125	0.041	0.324	−3.153	0.002	
TIPS	Garcia-Pagan, 2010	0.016	0.001	0.206	−2.907	0.004	
TIPS	Garcia-Pagan, 2013	0.044	0.011	0.161	−4.241	0.000	
TIPS	Monescillo, 2004	0.115	0.038	0.303	−3.318	0.001	
TIPS	Popovic, 2010	0.060	0.019	0.170	−4.621	0.000	
TIPS	Rudler, 2014	0.016	0.001	0.211	−2.883	0.004	
TIPS	Shi, 2014	0.188	0.101	0.211	−2.883	0.000	
TIPS		0.088	0.048	0.157	−6.994	0.000	



▶ **Fig. 3** Forest plot, rebleeding.

▶ **Table 2** Summary of pooled rates.

Outcomes	SEMS	TIPS
Pooled rate (95% confidence interval) 95% Prediction interval (PI), I^2 values		
Mortality	43.6% (28.6–59.8) PI: 18 to 73, 38	27.9% (16.3–43.6) PI: 2 to 88, 91
Immediate bleeding control	84.5% (74–91.2) PI: 50 to 97, 40	97.9% (87.7–99.7) PI: NA (due to limited number of studies)
Rebleeding	19.4% (11.9–30.4) PI: 6 to 50, 32	8.8% (4.8–15.7) PI: 2 to 33, 40
Technical success	88.3% (81.7–92.7) PI: 80 to 93, 0	91% (86.2–94.2) PI: 73 to 97, 26
All adverse events	36.9% (26–49.2) PI: 11 to 74, 52	41.4% (26.5–58.1) PI: 0.4 to 99, 29
Stent migration	31.8% (22–43.5) PI: 11 to 63, 41	NA

SEMS, self-expanding metal stent, TIPS: transjugular intrahepatic portosystemic shunt, NA: not applicable

The pooled rate of technical success with SEMS was 88.3% (95% CI 81.7–92.7) and with TIPS was 91% (95% CI 86.2–94.2). The pooled rate of all adverse events with SEMS was 36.9% (95% CI 26–49.2) and with TIPS was 41.4% (95% CI 26.5–58.1). The pooled rate of stent migration was 31.8% (95% CI 22–43.5). (Supplementary Fig. 2, 3 and 4) The pooled results are summarized in ▶ **Table 2**.

Validation of meta-analysis results

Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. On this analysis, no single study significantly affected the outcome or the heterogeneity.

Heterogeneity

We assessed dispersion of the calculated rates using the prediction interval (PI) and I^2 percentage values. The PI gives an idea of the range of the dispersion and I^2 tell us what proportion of the dispersion is true vs chance [19]. The calculated PIs and corresponding I^2 values are reported in ▶ **Table 2**. The calculated PI was wide except for the pooled rates of technical success. However, the I^2 heterogeneity was mild to moderate except for the morality rate with TIPS. This means that the reported pooled clinical outcomes may or may not be valid to the real-world scenario.

Publication bias

Based on visual inspection of the funnel plot as well as quantitative measurement that used the Egger regression test, there was evidence of publication bias (supplementary figure 5, Eggers 2-talied $P=0.04$). Further statistics using the fail-Safe N test and Duval and Tweedie's "Trim and Fill" test revealed that the impact of the possible publication bias appeared to be minimal and would not change the calculated estimate or the conclusion of this meta-analysis.

Quality of evidence

The quality of evidence was rated for results from the meta-analysis according to the GRADE working group approach [45]. Observational studies begin with a low-quality rating and based on the risk of bias, indirectness, heterogeneity, and publication bias, the quality of this meta-analysis would be considered as low-quality evidence.

Discussion

Our study demonstrates that use of SEMS is associated with a pooled all-cause mortality rate of 44 %, immediate bleeding control rate of 85 % and a rebleeding rate of 19 %. A recent multicenter study by Pfiesterer et al reported a mortality rate of 47 % with the use of SEMS in refractory EV bleeding and our results are on par with this study [9]. We report a pooled all-cause mortality rate of 28 % with TIPS. The mortality rates with SEMS and TIPS seemed comparable.

The pooled immediate bleeding control and rebleeding rates are the key findings of this study. 85 % of patients achieved immediate bleeding control with SEMS, whereas with TIPS 98 % of patients achieved immediate bleeding control. The pooled rebleeding rate with SEMS was 19 % and with TIPS was 9 %. Based on our comparison method, the probability that the proportion of patients undergoing TIPS having a successful outcome seemed to be more than the ones having a SEMS placed. The pooled rate of technical success with SEMS was 88 % and with TIPS was 91 %. Although the technical success rates were comparable, the prompt availability of emergent TIPS continues to be an issue at many centers due to limited resources and experienced personnel.

The Baveno VI recommendation on the use of SEMS in refractory EV hemorrhage is based on its favorable safety profile when compared to balloon-tamponade [3]. Our analysis of the adverse events with SEMS revealed a pooled rate of 37 % and was comparable to the pooled adverse event rate with TIPS, which was 41 %. Stent migration is a significant problem and our analysis revealed that the stent migrated in approximately one-third of the patients (31 %).

How does our study compare to other published reviews? The meta-analysis by McCarty and Njei reported a pooled bleeding control rate of 96 % [46]. The pooled outcomes reported in that study is of questionable validity due to the inclusion of studies that had overlapping cohorts (Hubmann 2006 with Zehetner 2008 and Hogan 2009 with Wright 2010) [32, 34, 43, 44]. Another meta-analysis by Marot et al., had similar limitation and only reported the mortality and adverse events [47]. Our study, on the contrary, has avoided studies with overlapping cohorts and we have presented the pooled results in perspective to the pooled outcomes of TIPS in refractory EV bleeding, thereby enabling a side-by-side comparison. The meta-analysis by Shao et al., report that SEMS may be considered in patients with EV bleeding refractory to conventional therapy and their pooled rates are comparable to this study [48]. The meta-analysis by Qi eta l on TIPS in acute EV bleeding reported that TIPS with covered stents might improve the overall survival of high-risk patients with acute EV bleeding [49]. The results are comparable to the pooled mortality rates reported in this study.

The strengths of this review are as follows: systematic literature search with well-defined inclusion criteria, careful exclusion of redundant studies, inclusion of good quality studies with detailed extraction of data and rigorous evaluation of study quality. Our pooled rates are calculated from 176 patients treated with SEMS and 398 patients treated with TIPS. There are limitations to this study, most of which are inherent to any meta-analysis. The included studies were not entirely representative of the general population and community practice, with most studies being performed in tertiary-care referral centers. Our analysis had studies that were retrospective in nature contributing to selection bias. It is practically impossible to compare SEMS to TIPS in refractory EV bleeding by RCT methods and a network meta-analysis is not possible due to lack of studies with a common comparator. Our study presents the results of SEMS and TIPS side by side, however, our analysis has the limitation of retrospective comparison and therefore we do not comment on the superiority and/ or inferiority of one modality to other. Nevertheless, our study is the best available estimate in literature thus far with respect to the clinical outcomes of SEMS and TIPS in refractory EV bleeding.

Conclusion

In conclusion, based on our meta-analysis, the use of SEMS in refractory EV bleeding demonstrates acceptable technical success and immediate bleeding control. However, the pooled mortality rate and rebleeding rate with TIPS seem to be lesser than SEMS. We, unfortunately, are unable to validate the results of comparison between the two modalities due to the limitations in our retrospective comparison methodology.

Competing interests

The authors declare that they have no conflict of interest.

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