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REVIEW

Performance of ultrasound for detection of transjugular intrahepatic portosystemic shunt dysfunction: a meta-analysis

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Abstract

Purpose Although ultrasound has been widely used to evaluate transjugular intrahepatic portosystemic shunts (TIPS) patency, several studies have reported conflicting data regarding its performance. Therefore, we aimed to evaluate performance of ultrasound for detection of TIPS dysfunction by performing a meta-analysis.

Methods Literature search was performed for studies evaluating ultrasound for TIPS dysfunction, stenosis, and occlusion using PubMed, EMBASE, Scopus, and Cochrane Library through February 2019. Pooled sensitivity, specificity, log diagnostic odds ratio (LDOR), and area under curve (AUC) of summary receiver-operating characteristic were calculated. Subgroup analyses were performed according to ultrasonographic criteria and type of stent.

Results In total, 21 studies were evaluated. Pooled sensitivity, specificity, and LDOR of ultrasound for detection of TIPS dysfunction were 0.82 (0.67, 0.93), 0.58 (0.46, 0.70), and 1.77 (1.20, 2.35). Pooled sensitivity, specificity, and LDOR for TIPS stenosis were 0.80 (0.69, 0.90), 0.80 (0.69, 0.91), and 2.83 (1.88, 3.78). Pooled sensitivity, specificity, and LDOR for TIPS occlusion were 0.96 (0.92, 0.99), 1 (0.99, 1.00), and 6.28 (4.96, 7.60). AUCs of ultrasound for TIPS dysfunction, stenosis, and occlusion were 0.77, 0.86, and 0.95, respectively.

Conclusions Although ultrasound had excellent performance for TIPS occlusion and acceptable performance for TIP stenosis, most studies utilized bare metal stent, and therefore, application to current practice is limited. Ultrasound for TIPS dysfunction in the setting of covered metal stent appeared to have acceptable sensitivity of 0.82, but limited specificity of 0.58 and low LDOR of 1.77. A new noninvasive tool is needed for detection of TIPS dysfunction in the era of covered metal stent.

Keywords Transjugular intrahepatic portosystemic shunt · Stents · Doppler ultrasonography · Cirrhosis · Portal hypertension

Introduction

Transjugular intrahepatic portosystemic shunts (TIPS) is an effective treatment for patients with cirrhosis and noncirrhotic portal hypertension who suffer from refractory ascites or variceal bleeding [1]. However, significant numbers of

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patients develop recurrent ascites or varices after the procedure due to TIPS dysfunction.

Historically, in the era of bare metal (BM) stent, several studies reported incidence of TIPS dysfunction to be as high as 60–80% at 2 years [2, 3]. TIPS dysfunction can be generally classified into early TIPS dysfunction due to malposition, compression, thrombosis, and late TIPS dysfunction due to pseudointimal hyperplasia [4]. Since the development of covered metal (CM) or polytetrafluoroethylene (PTFE) stent, several studies report 20–30% incidence of TIPS dysfunction at 2 years [2, 3]. Although the incidence of TIPS dysfunction from a CM stent is significantly lower than a BM stent, this number remains clinically important.

In order to accurately detect TIPS dysfunction, shunt venography along with portal pressure gradient (PPG) measurement is generally required. Although this method allows simultaneous TIPS revision when stenosis or occlusion is found, it is invasive and costly [5–7]. Therefore, Doppler ultrasonography has been widely used by hepatologists and radiologists to evaluate TIPS patency; however, several studies showed conflicting results regarding its performance [8, 9]. In addition, although several parameters have been suggested, there is no consensus regarding the best parameter. Moreover, most of the studies were also performed in the era of BM stent, when data on CM stents are more limited. Therefore, in this meta-analysis, we aim to evaluate performance of Doppler ultrasound for detection of TIPS dysfunction, stenosis, and occlusion and to evaluate for its performance in the setting of BM and CM stents.

Materials and methods

We conducted this systematic review and meta-analysis according to the guidelines provided by the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy [10], and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was adopted in the preparation of this manuscript [11].

Literature search

A literature search of PubMed, EMBASE, Scopus, and Cochrane Library was performed through February 2019. Search terms included “portosystemic shunt, transjugular intrahepatic” or “transjugular intrahepatic portosystemic shunt” and “ultrasonography Doppler” or “duplex ultrasound” or “duplex sonography” or “Doppler sonography.” Additional articles were manually searched from bibliographies of selected articles and pertinent review articles. The titles, abstracts, and full texts of the articles were reviewed by two independent reviewers (N.W. and P.P.). Abstracts from national and international meetings were reviewed, but eventually none were included due to lack of data.

Studies which met the following inclusion criteria were included for further analysis: (1) adult (≥ 18 year) with cirrhosis or noncirrhotic portal hypertension, (2) utilization of Doppler ultrasound as an index test, (3) TIPS dysfunction including stenosis and occlusion as a diagnosis of interest, and (4) utilization of venography and/or PPG measurement as a reference standard. If multiple publications derived from the same study population were identified, the most recent publications were used. All disagreements were resolved through joint decision after discussion between the two authors and a senior author. Articles in foreign language without English version were excluded.

Data extraction and quality assessment

Two authors independently extracted data from each study including characteristics of study, characteristics of study population, and results of study. Characteristics of study included first author, year, study design, country, start date, end date, type of stent, type of Doppler ultrasound, use of contrast, number of cases, post-TIPS ultrasonographic protocol, post-TIPS venography protocol, type of TIPS dysfunction, ultrasonographic criteria, and venographic criteria. Characteristics of study population included mean age, gender, indications for TIPS placement (presence of ascites/hydrothorax, bleeding, or Budd Chiari syndrome), Child–Pugh score, and etiology of cirrhosis. Results of study included prevalence of TIPS dysfunction, sensitivity, specificity, true positive, false positive, false negative, and true negative. True positive, false positive, false negative, and true negative values were obtained or calculated from results of each study. Quality assessment was independently performed according to QUADAS-2 by two authors [12]. The discrepancy between the two authors were resolved through joint decision after discussion between the two authors and the senior author.

Statistical analysis

R version 3.2.4 (R Core team 2013) was used for all statistical analysis. Due to discrepancy in venographic criteria of TIPS dysfunction between studies, we categorized the included studies into three categories according to type of TIPS dysfunction: (1) studies which defined TIPS dysfunction as both stenosis and occlusion without separation between the two were classified as “TIPS dysfunction”; (2) studies which clearly defined TIPS dysfunction as stenosis without occlusion were classified as “TIPS stenosis”; and (3) those which clearly defined TIPS dysfunction as occlusion without stenosis were classified as “TIPS occlusion.” We then evaluated the performance of Doppler ultrasound in detection of TIPS dysfunction, stenosis, and occlusion separately. When more than one cutoff was available, the most commonly used cutoff defined in other studies was selected. If no previous cutoff was described in other studies, the cutoff with the highest Youden's index was selected to provide the best overall performance. This is to prevent bias caused by authors purposefully selecting certain cutoffs to increase pooled sensitivity or specificity [13]. Pooled sensitivity and specificity were calculated along with 95% confidence interval. Log diagnostic odd ratios (LDORs) were calculated using Dersimonian and Laird method which adjusted for heterogeneity between studies [14]. Summary receiver-operating curve (SROC) was calculated and constructed based on the bivariate analysis of sensitivity and specificity, described by Reitsma et al. [15]. We calculated both full area under the curve (AUC) and partial AUC; however, due to significant heterogeneity between studies, full AUC was utilized to evaluate an overall test performance as previously suggested by Walter et al. [16]. Subgroup analyses were performed according to type of stent and diagnostic criteria. Quality of study was defined as high if biases were low in all domains of the QUADAS-2. I^2 statistic was utilized to address heterogeneity between studies. Heterogeneity was considered to be significant if I^2 value was $\geq 50\%$. Publication bias was explored based on effective sample sizes (ESSs), using Deeks' funnel plot and a test for asymmetry by a regression of LDOR against $(1/\text{ESS})^{1/2}$, weighting by ESS [17]. The significant publication bias was defined by the p value less than 0.10 from the test for asymmetry.

Results

A total of 399 articles were found using the previously outlined search criteria. Of these, 70 studies were evaluated for eligibility. Two studies (Micol et al. and Uggowitzer et al.) with two cohorts utilizing intravenous contrast during ultrasonography were excluded because of insufficient studies to perform meta-analysis. Ultimately, there were 21 studies included in the analysis. Overall, 11 studies/14 cohorts evaluated ultrasound for detection of TIPS dysfunction, 10 studies/10 cohorts for TIPS stenosis, and 10 studies/11 cohorts for TIPS occlusion (Fig. 1).

Characteristics of studies and study population

Total of 1406 subjects with 2207 comparisons of ultrasonography and venography were analyzed. There were

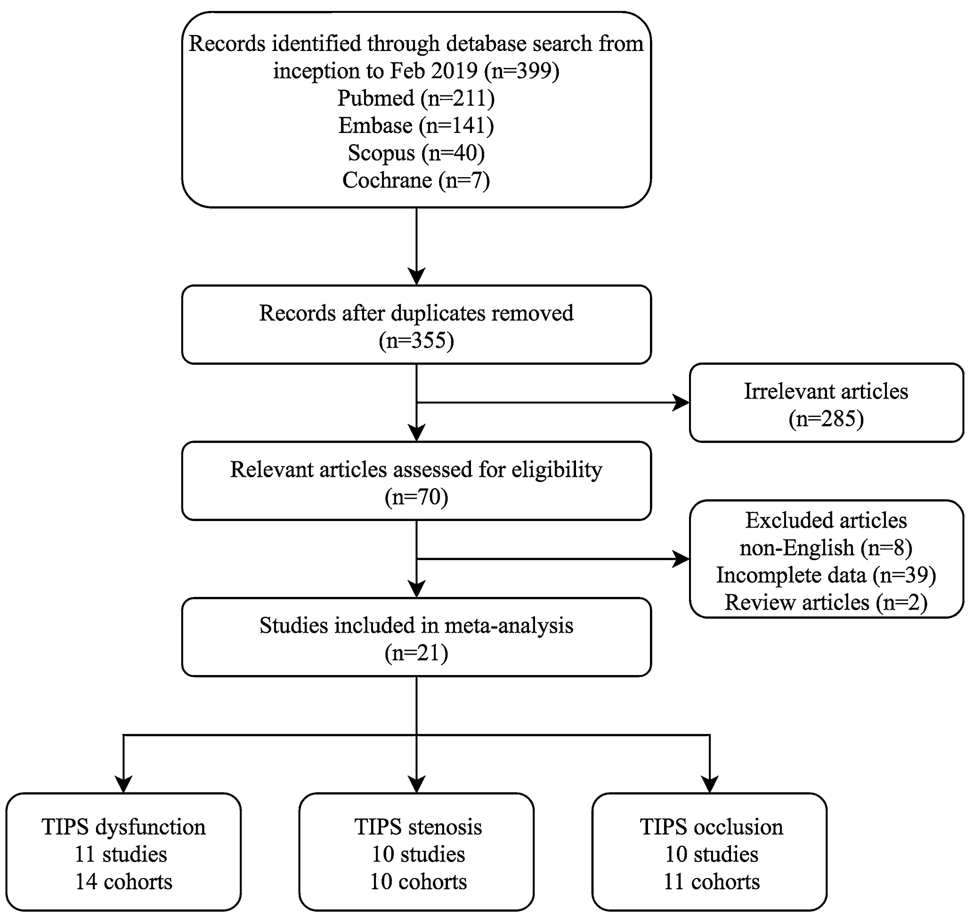

Fig. 1 A flowchart demonstrating the study selection used

1039 comparisons in the analysis of TIPS dysfunction, 1032 comparisons in TIPS stenosis, and 1233 comparisons in TIPS occlusion. Table 1 demonstrates study characteristics of each cohort including year, country, study design, start date, end date, type of stent, type of ultrasound, follow up protocol, and venographic access. Among studies in the TIPS dysfunction group, there were six cohorts using BM, seven cohorts using CM, and one cohort with both types. Among studies in the TIPS stenosis group, there were eight cohorts using BM, one cohort using both CM and BM, and one cohort which did not specify stent type. In the TIPS occlusion group, there were nine cohorts using BM, one cohort using both, and one cohort which did not specify stent type. Characteristics of study population of each cohort and detail regarding post-TIPS follow up protocol for ultrasonography and venography are shown in supplementary Tables 1 and 2, respectively. Table 2 demonstrates extracted data from each cohort for TIPS dysfunction, stenosis, and occlusion including type of stent, simplified ultrasonographic criteria, venographic criteria, and performance of ultrasound. Details of ultrasonographic criteria and extracted data for TIPS dysfunction and stenosis are shown in supplementary Tables 3 and 4, respectively.

Performance of ultrasound

Table 3 demonstrates results of overall performance of ultrasound for detection of TIPS dysfunction, stenosis, and occlusion along with subgroup analyses. Graphical representation of pooled sensitivity, specificity, and LDOR for TIPS dysfunction, stenosis, and occlusion are shown in supplementary Figs. 1–3, 4–6, and 7–9, respectively.

For TIPS dysfunction, pooled sensitivity, specificity, and LDOR were 0.82 (0.67, 0.93), 0.58 (0.46, 0.70), and 1.77 (1.20, 2.35), respectively. AUC of ultrasound for TIPS dysfunction was 0.77 (Fig. 2a). In the subgroup analyses, pooled sensitivity of composite criteria was 0.83 (0.71, 0.94) followed by portal vein velocity (0.58 [0.39, 0.84]) and peak stent velocity (0.54 [0.21, 0.87]). Pooled specificity of in-stent V_{max} was 0.78 (0.71, 0.85) and pooled specificity of portal vein velocity was 0.78 (0.67, 0.90) while pooled specificity of composite criteria was only 0.59 (0.41, 0.76). LDORs of composite criteria, in-stent V_{max}, and portal vein velocity were low (1.95 [1.17, 2.72], 1.60 [− 0.07, 3.26], and 1.66 [0.98, 2.35]). According to stent type, pooled specificity of ultrasound was similar between BM and CM stents (0.57 [0.45, 0.70] vs 0.57 [0.35, 0.79], while pooled sensitivity and LDOR of ultrasound for BM was higher than CM (0.90 [0.85, 0.94] vs 0.79 [0.65, 0.93] and 2.08 [1.23, 2.94] vs 1.63 [0.67, 2.60]) although not statistically significant. For TIPS stenosis, pooled sensitivity, specificity, and LDOR were 0.80 (0.69, 0.90), 0.80 (0.69, 0.91), and 2.83 (1.88, 3.78) while AUC was 0.86 (Fig. 2b). Subgroup analysis according to type of stent was not possible due to the absence of studies utilizing CM stents. According to diagnostic criteria, performances of composite criteria and in-stent V_{max} were similar (Table 3). For TIPS occlusion, ultrasound had pooled sensitivity of 0.96 (0.92, 0.99), pooled specificity of 1 (0.99, 1.00), and LDOR of 6.28 (4.96, 7.60) with AUC of 0.95 (Fig. 2c).

Quality assessment and publication bias

Quality assessment of each study according to the guidelines by QUADAS-2 is shown in supplementary Table 5. Concern for biases regarding patient selection, index test, reference standard, flow, and timing of imaging was overall low except for a study by Engstrom, which had high patient selection bias. By utilizing Deeks' funnel plots, no significant publication bias was found among studies evaluating ultrasound for TIPS dysfunction, TIPS stenosis, and TIPS occlusion ($p = 0.30$, 0.54, and 0.21) (Fig. 3).

Discussion

Our meta-analysis demonstrated excellent performance of ultrasound for detection of TIPS occlusion with high sensitivity (0.96 [0.92, 0.99]), specificity (1.00 [0.99, 1.00]), and LDOR (6.28 [4.96, 7.60]). When ultrasonographic criteria was utilized to detect TIPS dysfunction (without separation between stenosis and occlusion), specificity and LDOR were low (0.58 [0.46,0.70] and 1.77 [1.20, 2.35]) while sensitivity was acceptable (0.82 [0.67,0.93]). Contrarily, when ultrasound was utilized to specifically detect TIPS stenosis, sensitivity, specificity, and LDOR were acceptable (0.80 [0.69, 0.90], 0.80 [0.69, 0.91], and 2.83 [1.88, 3.78]). Specificity of ultrasound was also higher for detection of TIPS stenosis than dysfunction (0.80 [0.69, 0.91] vs 0.58 [0.46, 0.70]).

Although the gold standard for evaluation of TIPS patency is venography with PPG measurement, ultrasound is a more cost-effective method and is generally performed to simultaneously screen for hepatocellular carcinoma. As a result, ultrasound has been widely utilized by hepatologists and radiologists to evaluate TIPS patency. Previous studies, however, have shown conflicting data. For example, studies by Haskal and Uggowitzer reported sensitivity of ultrasound to be approximately 50% for TIPS stenosis while Fanelli reported sensitivity of 90% for TIPS dysfunction [18–20]. Furthermore, most studies were performed in the era of BM stent while, currently, CM stent is the standard for TIPS procedure due to lower incidence of TIPS dysfunction.

In this study, we were able to successfully evaluate performance of ultrasound for evaluation of TIPS patency by categorizing the studies into three categorizes according to type of venographic diagnoses: TIPS dysfunction

Table 1 Study characteristics of each cohort and study

Author	Year	Country	Design	Start date	End date	Stent type	US type	Routine US	Routine venography	Venographic access
Abraldes_1 [5]	2005	Spain	Retrospective	Jul 1995	Jul 1998	BM	CDUS	Yes	Yes	Jugular, femoral
Abraldes_2 [5]	2005	Spain	Prospective	Jun 1999	Mar 2001	BM	CDUS	Yes	Yes	Jugular, femoral
Abraldes_3 [5]	2005	Spain	Prospective	2001	2004	CM	CDUS	Yes	Yes	Jugular, femoral
Benito [6]	2004	Spain	Retrospective	NA	NA	NA	CDUS	Yes	Yes	Jugular, femoral
Bureau [2]	2007	France	Prospective	Feb 2000	Apr 2002	Mix	NA	Yes	Yes	NA
Chong [24]	1993	USA	NA	NA	NA	BM	CDUS	Yes	Yes	Antecubital, jugular, femoral
Dodd [25]	1995	USA	Prospective	Sep 1991	Sep 1992	BM	CDUS	Yes	Yes	Jugular
Engstrom [21]	2013	USA	Retrospective	Nov 2004	Dec 2010	BM CM	CDUS	Yes	No	Jugular
Fanelli [20]	2011	Italy	Prospective	Jan 2000	Jan 2009	CM	CDUS	Yes	No	NA
Feldstein [8]	1996	USA	Prospective	Sep 1990	Dec 1993	BM	CDUS	Yes	Yes	Antecubital, jugular, femoral
Ferguson [26]	1995	UK	Prospective	NA	NA	BM	CDUS	NA	NA	Jugular
Foshager [1]	1995	USA	NA	NA	NA	BM	CDUS	Yes	No	Jugular
Haskal [18]	1997	USA	Prospective	Jun 1991	Jul 1994	BM	CDUS	Yes	Yes	Antecubital, jugular, femoral
Kanterman [27]	1997	USA	Prospective	May 1991	Mar 1995	BM	CDUS	Yes	Yes (14 patients)	NA
Kimura [28]	1996	Japan	Retrospective	Feb 1992	Mar 1994	Mix	CDUS	Yes	Yes	NA
Klinger [29]	2018	Germany	Retrospective	Jan 2007	Jun 2014	CM	CDUS	Yes	No	Jugular
Micol [23]	2011	France	Retrospective	Feb 2001	Sep 2008	Mix	CDUS	Yes	No	Jugular
Murphy [30]	1998	USA	Prospective	Nov 1991	Mar 1996	BM	CDUS	Yes	Yes	Jugular, femoral, basilic
Nicolas [31]	2017	France	Prospective	Feb 2008	Jul 2009	CM	CDUS	Yes	Yes	NA
Owen [22]	2016	USA	Retrospective	Jan 2003	Dec 2015	CM	CDUS	Yes	No	Jugular
Uggowitzer [19]	1998	Austria	Prospective	NA	NA	BM	CDUS/PDUS	Yes	Yes	Jugular
Young [32]	2017	USA	Retrospective	Jan 2005	Dec 2015	CM	Conventional	Yes	No	NA
Zizka [33]	2000	Czech Republic	Retrospective	Feb 2000	Apr 2002	BM	CDUS	Yes	No	Jugular

US ultrasonography, *NA* not available, *BM* bare metal, *CM* covered metal, *CDUS* color Doppler ultrasonography, *PDUS* power Doppler ultrasonography

Table 2 Extracted data from cohorts and studies evaluating ultrasonography for TIPS dysfunction, stenosis, and occlusion

Study	Stent type	Ultrasonographic criteria	Venographic criteria[a]	Se	Sp	TP	FP	FN	TN
Dysfunction									
Abraldes_1 [5]	BM	Composite	PPG > 12 mmHg	90	45	51	33	6	27
Abraldes_2 [5]	BM	Composite	PPG > 12 mmHg	82	56	18	24	4	31
Abraldes_3 [5]	CM	Composite	PPG > 12 mmHg	100	59	8	14	0	20
Bureau [2]	Mix	Portal vein velocity	PPG > 12 mmHg, > 50% stenosis	62.5	68.4	20	24	12	52
Dodd [25]	BM	Composite	PPG > 15 mmHg	94	76.9	15	3	1	10
Engstrom_BM [21]	BM	In-stent V_{max}	PPG > 12 mmHg	77.3	35	17	13	5	7
Engstrom_CM [21]	CM	In-stent V_{max}	PPG > 12 mmHg	76.5	42.4	39	19	12	14
Fanelli [20]	CM	Changes in In-stent V_{max}	PPG > 12 mmHg	90	75	18	15	2	45
Ferguson [26]	BM	In-stent V_{max}	PPG ≥ 12 mmHg	100	63.6	6	4	0	7
Kanterman [27]	BM	Composite	PPG > 15 mmHg or > 50% stenosis	92	72	36	7	3	18
Klinger [29]	CM	Composite	PPG > 12 mmHg	89.5	81.5	17	5	2	22
Nicolas [31]	CM	Composite	PPG ≥ 12 mmHg or > 50% stenosis	39.1	87.1	31	18	48	121
Owen [22]	CM	Composite	PPG > 12 mmHg, stenosis	85	50	17	16	3	16
Young [32]	CM	Composite	PPG > 12 mmHg	80	4	28	24	7	1
Stenosis									
Benito [6]	NA	Composite	PPG > 15 mmHg or 50% stenosis	82	55	20	168	4	206
Chong [24]	BM	In-stent V_{max}	NA	100	93	8	6	0	73
Dodd [25]	BM	Changes in In-stent V_{max}	PPG > 15 mmHg	93	77	14	3	1	11
Feldstein [8]	BM	In-stent V_{max}	> 50% stenosis	78	99	25	1	7	71
Foshager [1]	BM	In-stent V_{max}	PPG > 15 mmHg or > 50% stenosis	100	50	9	2	0	1
Haskal [18]	BM	Composite	PPG > 15 mmHg	54	92	15	7	13	84
Micol [23]	Mix	Composite	PPG > 12 mmHg or > 50% stenosis	58.8	85.7	20	4	14	24
Murphy [30]	BM	Mid-shunt velocity	PPG ≥ 15 mmHg	83	75	21	7	4	21
Uggowitzer [19]	BM	Composite	PPG ≥ 15 mmHg or 50% stenosis	47	50	8	4	9	4
Zizka [33]	BM	Composite	PPG > 12 mmHg	93.6	87.9	103	4	7	29
Occlusion									
Benito [6]	NA	Absence of flow	Occlusion	100	100	9	0	0	413
Chong [24]	BM	Absence of flow	Occlusion	100	98.7	4	1	0	78
Dodd [25]	BM	Absence of flow	Occlusion	100	100	1	0	0	28
Feldstein [8]	BM	Absence of flow	Occlusion	96	99	25	1	1	192
Foshager_1 [1]	BM	Absence of flow	Occlusion	100	66.7	5	1	0	2
Foshager_2 [1]	BM	Absence of flow	Occlusion	100	100	2	0	0	63
Haskal [18]	BM	Absence of flow	Occlusion	100	100	8	0	0	106
Kimura [28]	BM	Absence of flow	Occlusion	92	89	8	4	1	44
Micol [23]	Mix	Absence of flow	Occlusion	100	100	20	0	0	42
Uggowitzer [19]	BM	Absence of flow	Occlusion	100	89	4	3	0	24
Zizka [33]	BM	Absence of flow	Occlusion	96.2	100	25	0	1	117

Se sensitivity, *Sp* specificity, *TP* true positive, *FP* false positive, *FN* false negative, *TN* true negative, V_{max} maximum velocity, *BM* bare metal, *CM* covered metal, *PPG* portal pressure gradient

[a]The studies in the dysfunction group did not report or separate patients with TIPS occlusion in the analyses while the studies in the stenosis group clearly reported and separated analyses of patients with stenosis and occlusion separately

(without separation of stenosis and occlusion), TIPS stenosis, and occlusion. By following this methodology, we demonstrated that ultrasound was an excellent tool to diagnose TIPS occlusion with high sensitivity, specificity, and LDOR. Its performance also appeared to be consistent through all studies as reflected by very low level of heterogeneity. Nonetheless, it is important to note that 9 out of 11 cohorts in the analysis utilized BM stents. Therefore, applying these findings to current practice which CM stent is the standard remains debatable. Similarly, although the performance of ultrasound for detection of TIPS stenosis appeared to be acceptable with sensitivity of 0.80

Table 3 Performance of ultrasonography in detection of TIPS dysfunction, stenosis, and occlusion with subgroup analyses according to diagnostic criteria and stent type

Cohort (*n*)	Se (95%CI)	I^2 (%)	Sp (95%CI)	I^2 (%)	LDOR (95%CI)	I^2 (%)	AUC
Dysfunction							
Overall (14)	0.82 (0.67, 0.93)	83.1	0.58 (0.46, 0.70)	92.4	1.77 (1.20, 2.35)	24.9	0.77
By diagnostic criteria							
Composite criteria (9)	0.83 (0.71, 0.94)	88.5	0.59 (0.41, 0.76)	94.7	1.95 (1.17, 2.72)	28.9	0.79
In-stent V_{max} (4)	0.54 (0.21, 0.87)	95.4	0.78 (0.71, 0.85)	0	1.60 (− 0.07, 3.26)	0	0.77
Portal vein velocity (4)	0.58 (0.39, 0.78)	85.1	0.78 (0.67, 0.90)	64.5	1.66 (0.98, 2.35)	1.4	0.76
Stent type							
Bare metal (6)	0.90 (0.85, 0.94)	0	0.57 (0.45, 0.70)	65.0	2.08 (1.23, 2.94)	4.8	0.84
Covered metal (7)	0.79 (0.65, 0.93)	87.9	0.57 (0.35, 0.79)	96.5	1.63 (0.67, 2.60)	32.2	0.76
Stenosis							
Overall (10)	0.80 (0.69, 0.90)	85.1	0.80 (0.69–0.91)	94.4	2.83 (1.88, 3.78)	10.8	0.86
By diagnostic criteria							
Composite criteria (5)	0.69 (0.51, 0.87)	88.6	0.76 (0.60–0.93)	94.3	2.28 (0.97, 3.59)	19.8	0.82
In-stent V_{max} (6)	0.77 (0.62, 0.85)	83.2	0.87 (0.78–0.95)	91.3	2.88 (1.64, 4.12)	7.8	0.85
Occlusion							
Overall (11)	0.96 (0.92, 0.99)	0	1.00 (0.99–1.00)	4.03	6.28 (4.96, 7.60)	0	0.95

CI confidence interval, *Se* sensitivity, *Sp* specificity, *LDOR* log diagnostic odds ratio, *AUC* area under the curve, V_{max} maximum velocity

(0.69–0.90) and specificity of 0.80 (0.69–0.91), 8 out of 10 studies in this analysis utilized BM stents. More importantly, ultrasonographic criteria was also derived from studies in the era of BM stents; therefore, applying the same criteria for BM stent to CM stent might not result in the same conclusion [21]. Therefore, more studies are necessary to evaluate performance of ultrasound for detection of TIPS occlusion and stenosis in the setting of CM stent.

Among studies which evaluated performance of ultrasound for detecting TIPS dysfunction without separating TIPS stenosis and occlusion, overall performance of ultrasound appeared to be low with specificity of 0.58 (0.46, 0.70) and LDOR of 1.77 (1.20, 2.35) despite acceptable sensitivity of 0.82 (0.67, 0.93). According to the subgroup analyses, this could potentially be contributed by low performance of composite criteria for TIPS dysfunction given lower specificity compared to in-stent V_{max} (0.51 [0.32, 0.69] vs 0.78 [0.71, 0.85]). In theory, the performance of ultrasound for detection of TIPS dysfunction was expected to be better than TIPS stenosis since studies in the TIPS dysfunction did not separate patients with TIPS occlusion. However, our study showed that specificity of ultrasound for TIPS dysfunction was noticeably lower than that of TIPS stenosis (0.58 [0.46, 0.70] vs 0.80 [0.69, 0.91]). Although the reason is unclear, we postulated that this could be due to larger number of cohorts in the TIPS dysfunction group utilized composite criteria as reflected by lower specificity in the studies utilizing composite criteria compared to single criteria such as in-stent V_{max} or portal vein velocity.

The most applicable and clinically relevant data are likely derived from the subgroup analysis of studies evaluating performance of ultrasound for TIPS dysfunction in the setting of CM stent since CM stent is the current standard of care. For CM stent, ultrasound had low performance for detection of TIPS dysfunction with specificity of 0.58 (0.46, 0.70) and LDOR 1.77 (1.20, 2.35). Nonetheless, sensitivity appeared to be acceptable (0.82 [0.67, 0.93]). This suggests that ultrasound could potentially be used as an acceptable screening tool for TIPS dysfunction in the setting of CM stent, but it is not a perfect tool due to limited specificity and LDOR. Furthermore, the role of ultrasound for detection of TIPS dysfunction has recently been further challenged, and other tools have been suggested, such as clinical symptoms of portal hypertension, contrast-enhanced ultrasound, and other cross-sectional imaging. For instance, Owen et al. demonstrated that clinical symptoms had 80% sensitivity and 25% specificity while ultrasound had 85% sensitivity and 50% specificity [22]. In this current study, we also attempted to evaluate performance of contrast-enhanced ultrasound for detection of TIPS dysfunction; however, the number of studies was not adequate for meta-analysis. A study by Micol and Uggowitzer has also demonstrated improved performance of contrast-enhanced ultrasound; however, it has not been widely studied and utilized [19, 23].

When comparing the performance of ultrasound in the settings of CM with BM stents, sensitivity and LDOR of ultrasound for CM stent appeared to be lower (0.79 [0.65, 0.93] vs 0.90 [0.85, 0.94] and 1.63 [0.67, 2.60] vs 2.08 [1.23, 2.94]). This raised concern regarding the effect of

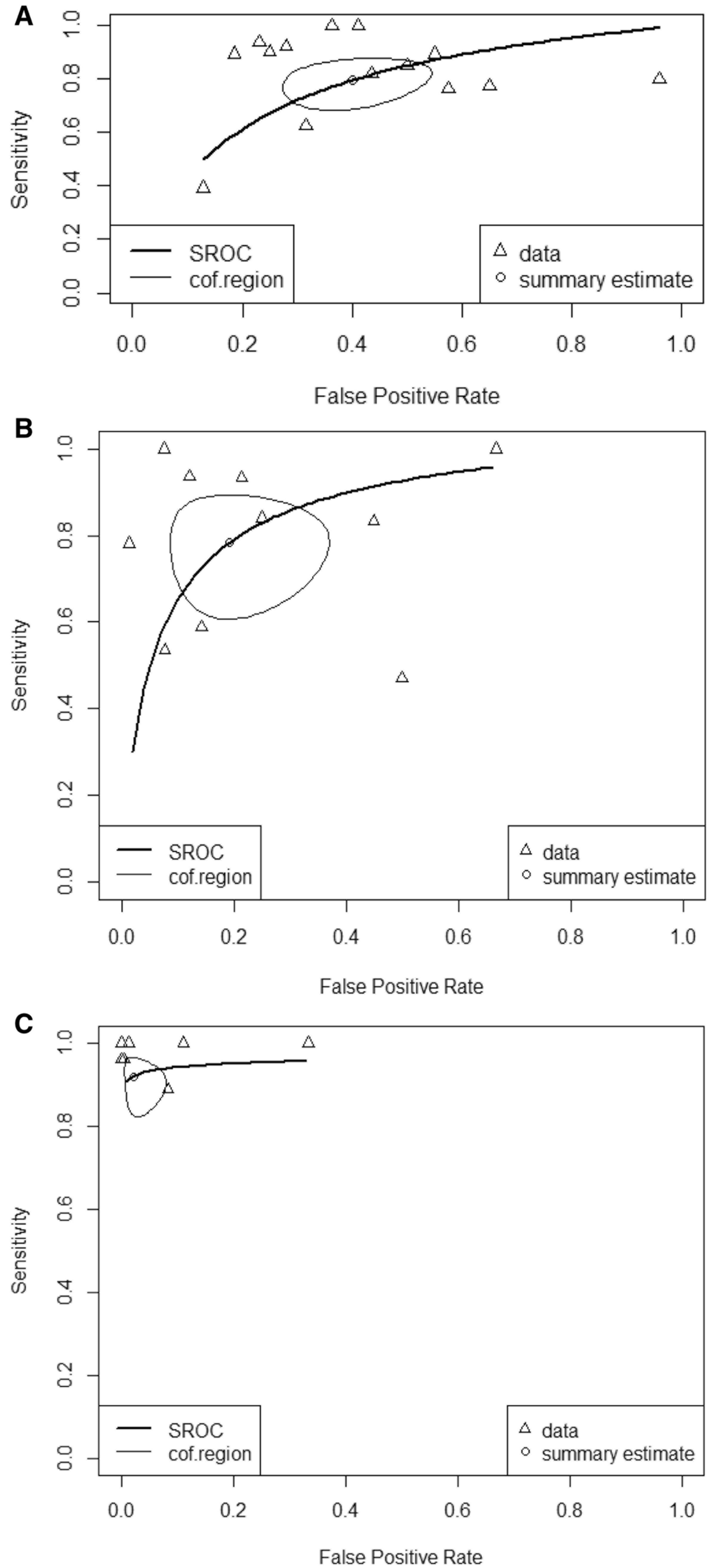

Fig. 2 SROC demonstrating performance of ultrasound for detection of TIPS dysfunction (**a**), stenosis (**b**), and occlusion (**c**)

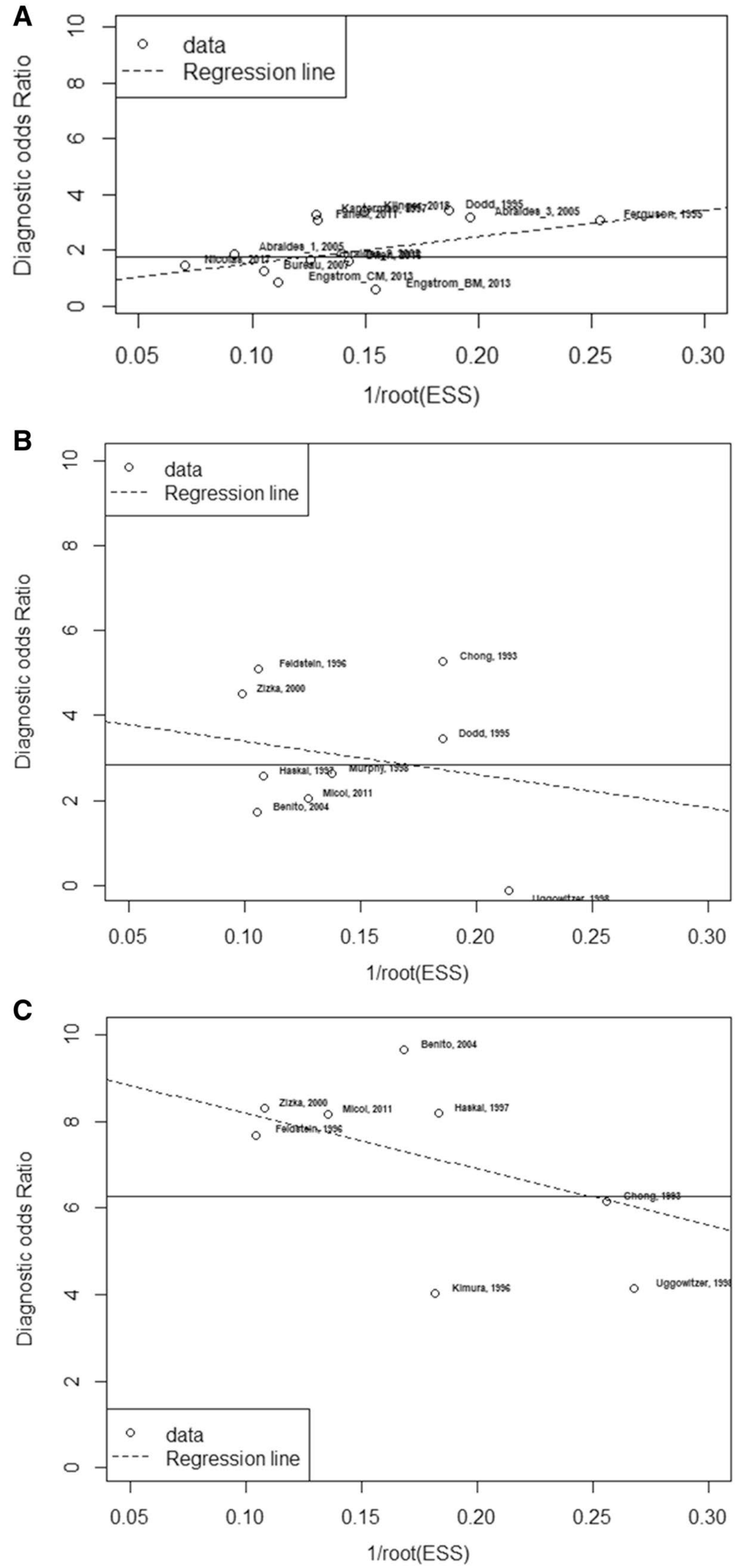

Fig. 3 Deeks funnel plots evaluating publication bias for TIPS dysfunction (**a**), stenosis (**b**), and occlusion (**c**) ($p = 0.30$, 0.54, and 0.21)

stent type on ultrasound performance as previously mentioned in other studies. However, it is impossible to conclude that CM lowers ultrasound performance considering the differences between sensitivity and LDOR were not statistically significant.

In summary, although ultrasound appeared to have an excellent performance for detection of TIPS occlusion and acceptable performance for detection of TIPS stenosis, the findings were limited to BM stent, and applicability to CM stent remains controversial. In the setting of CM stent, sensitivity appeared to be acceptable but specificity and LDOR were low suggesting that ultrasound is not an ideal tool. We believe that ultrasound could still be used to detect TIPS occlusion but the role of ultrasound after TIPS occlusion is ruled out is very limited. Therefore, venography should be performed when clinical suspicion is high. Further studies are needed to evaluate performance of ultrasound for detection of TIPS occlusion in the setting of BM, and a new noninvasive tool is needed for detection of TIPS dysfunction or stenosis.

The main strength of our meta-analysis is the inclusion of a large number of patient populations who have undergone TIPS. Consequently, this provides a closer representation of performance of ultrasound for detection of TIPS dysfunction in real life. We were also able to further categorize studies according to description of TIPS dysfunction: dysfunction, stenosis, and occlusion. Publication bias according to Deek's funnel plots was also not significant for all analyses. Regardless, our study has several weaknesses pertaining to the characteristic of the studies. First, there were differences in ultrasonographic criteria, cutoffs, and venographic criteria among studies. There was also no consensus regarding appropriate cutoffs for each parameter. Most importantly, approximately 2/3 of the studies performed venography on routine basis, and therefore, these studies could potentially over-diagnose patients with TIPS dysfunction or stenosis without clinical recurrence of portal hypertension. In conclusion, ultrasound has excellent performance for TIPS occlusion and decent performance for TIPS stenosis, but application to current practice is limited since most of the included studies utilized BM stents, whereas CM stents are now used.

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Author contributions WM, HS, and PP participated in the study design. Data extraction was performed by WM and PP, while quality assessment was performed by ME and NW. TI performed statistical analyses. WM, JS, and AB participated in the manuscript preparation.

Compliance with ethical standards

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